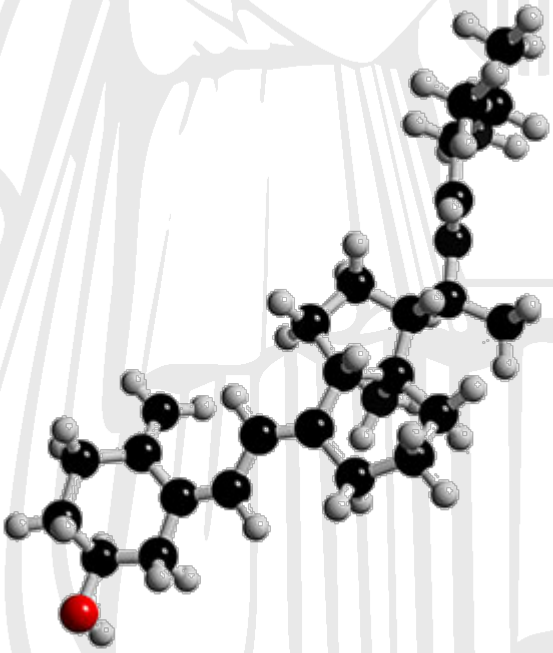
INTAKE OF VITAMIN D IN RELATION TO COGNITION IN THE ELDERLY

The Hordaland Health Study



Master Thesis by

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Oslo, September 2010

Linn Therese Larsen

Summary

Background: Increasing evidence suggests that vitamin D may be protective in the development of cognitive impairment and dementia in older subjects.

Objective: The overall objective was to examine the cross-sectional relationship between intake of vitamin D and cognitive performance.

Design: The subjects (n=1916), aged 70-74 years, were recruited from the general population in Western Norway and underwent cognitive testing. The cognitive test battery included the Kendrick Object Learning Test, Trail Making Test part A, and modified versions of the Digit Symbol Test, Block design, Mini mental State Examination and Controlled Oral Word Association Test. Data on dietary habits were collected via a food frequency questionnaire. Poor cognitive performance was defined as the lowest 10^{th} percentile for all of the tests, except the TMT-A were the 90^{th} percentile was used as a cut-off.

Results: Sixty-four percent of the population did not meet the Nordic recommendations of vitamin D intake (≥10 µg/d). Of those that took cod liver oil as a supplement, 76.1% reached the recommended intake of vitamin D. Fish was the most important food source of vitamin D contributing with 38.3% of the total intake of vitamin D. Multivariate linear regression analyses showed that the S-task (verbal fluency) and KOLT (episodic memory) were significantly associated with intake of vitamin D. Logistic regression analyses showed that the risk of scoring poorly on the KOLT was significantly increased when the intake of vitamin D was low (≤3.57µg/d) . Intake of cod liver oil was not associated with KOLT score. For non-users of cod liver oil the risk of scoring poorly on the KOLT increased when the intake of lean fish was low (0.1 g/d – 25.0 g/d, $P = 0.027$).

Conclusions: In the present population consisting of elderly from the western part of Norway, cod liver oil supplementation was effective in achieving recommended intake levels of vitamin D. Even though the population had a high intake of vitamin D-

containing foods compared to other studies, a high proportion of the individuals were not able to meet the Nordic recommendations (≥10 μg/d). A diet low in vitamin D was associated with a lower score on a verbal fluency test as well as an episodic memory test. In non-users of cod liver oil, episodic memory was negatively affected by a low intake of lean fish. Fish as a food item or dietary pattern may be more protective when it comes to cognitive decline than vitamin D as a single nutrient.

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Abbreviations

25(OH)D	25-hydroxyvitamin D (Cholecalciferol, vitamin D_3)
$1,25(OH)_2D_3$	1,25-dihydroxyvitamin D (Calcitriol)
ApoE	Apolipoprotein E
BMI	Body Mass Index
CI	Confidence Interval
CVD	Cardiovascular disease
DBP	Vitamin D binding protein
FFQ	Food Frequency Questionnaire
HADS	Hospital Anxiety and Depression Scale
HHS	Hordaland Homocysteine Study (1992-1993)
HUSK	Hordaland Health Study (1997-1999)
iNOS	Inducible nitric oxide synthase
IU	International Unit
kJ	Kilo Joules
KOLT	Kendrick Object Learning Test
m-BD	Modified version of the Block Design test
m-DST	Modified version of the Digit Symbol test
m-MMSE	Modified version of the Mini Mental State Examination
NNR	Nordic Nutrition Recommendation

OR	Odds Ratio
PAL	Physical activity level
PTH	Parathyroid hormone
PUFA	poly-unsaturated fatty acid
RDA	Recommended Daily Allowance
S-task	Abridged version of the Controlled Oral Word Association (COWAT)
SD	Standard Deviation
SE	Standard Error
tHcy	Total homocysteine
TMT-A	Trail Making Test part A
VDR	Vitamin D receptor
VDR-KO	Vitamin D receptor knock-out
Vitamin D_2	Ergocalciferol
UV	Ultra violet

1. Introduction

1.1 Vitamin D

1.1.1 Bioactivation

Vitamin D is a pro-hormone that is produced in the skin through a photolytic process induced upon exposure to sunlight (UVB 290-320 nm) [1]. There are two types of vitamin D; cholecalciferol (D_3) and ergocalciferol (D_2). Vitamin D_3 is produced in the skin, whereas vitamin D_2 is derived from plants and yeast. In the production of vitamin D_3, 7-dehydrocholesterol in cell membranes is converted to pre-vitamin D_3, which is then slowly converted to vitamin D_3 [2]. The bio-activation of vitamin D starts in the liver where vitamin D is hydroxylated at carbon 25 by 25-hydroxylase (a hepatic cytochrome P-450) (**Figure 1**). The hydroxylation reaction is poorly regulated and the levels of 25(OH)D increase in proportion to vitamin D intake [3]. For this reason, in addition to having a long half-life (3 weeks) 25(OH)D is used as an indicator for vitamin D status [1]. After formation of 25(OH)D has taken place, the formation of $1,25(OH)_2D_3$ (calcitriol) occur in the kidney through the action of 1α-hydroxylase [4] (Figure 1). The high potency of $1,25(OH)_2D_3$ in elevating serum calcium and phosphate levels requires a mechanism to stop its activity. This is accomplished within more or less all target cells by the $1,25(OH)_2D_3$-inducible vitamin D 24-hydroxylase [4].

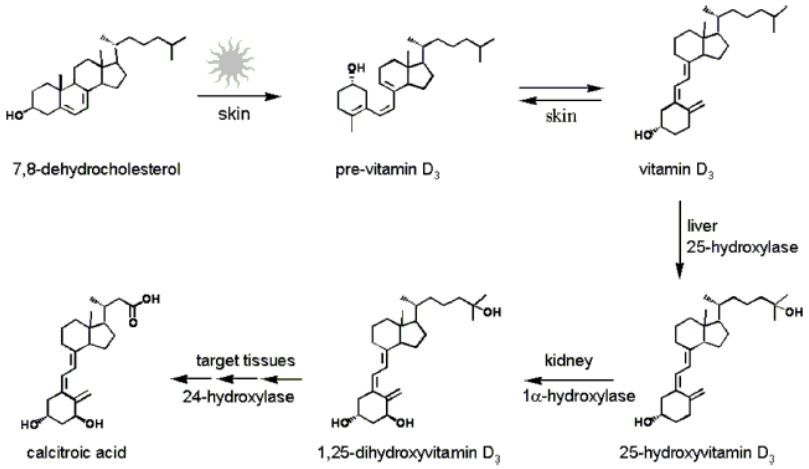


Figure 1. Adapted from Dusso et al. 2005

1.1.2 Transport of vitamin D

Vitamin D metabolites are lipophilic molecules with low aqueous solubility that are transported in the circulation bound to plasma proteins [4]. The most important of these carrier proteins is the vitamin D binding protein (DBP). Plasma levels of DBP are 20 times higher than the total amount of vitamin D metabolites [5], and the majority of 25(OH)D and $1,25(OH)_2D_3$ are bound to DBP (80-90%) and albumin (10-20%), while a tiny fraction is free in plasma [6].

Entry of 25(OH)D into the proximal tubule cells in the kidneys is not by diffusion across the basolateral surface but by receptor-mediated uptake of DBP in the brush border [7]. Once inside the cells, DBP is degraded, releasing 25(OH)D for metabolism by 1α-hydroxylase or 24-hydroxylase [8].

1.1.3 Functions of vitamin D

Vitamin D has several different functions in the body. They are usually classified into genomic and non-genomic actions and classical and non-classical functions.

Genomic actions

Most of the biological activities of $1,25(OH)_2D_3$ require a high-affinity receptor, the vitamin D receptor (VDR), a member of the superfamily of nuclear receptors for steroid hormones [9]. Like the other members of the steroid receptor family, the VDR acts as a ligand-activated transcription factor [10]. The major steps in which VDR regulate gene transcription include ligand binding to the ligand binding domain of the VDR, heterodimerization with retinoic X receptor, binding of the heterodimer to the vitamin D responsive element in the promoter region of vitamin D responsive gene, and recruitment of VDR-interacting nuclear proteins into the transcriptional pre-initiation complex [10]. This process ultimately results in either an enhancement or a suppression of the rate of gene transcription by the VDR [11].

Non-genomic actions

The active form of vitamin D can also bring forth responses that are too rapid to involve changes in gene expression. These responses appear to be mediated by cell surface receptors and second messengers [4]. $1,25(OH)_2D_3$ can rapidly stimulate phosphoinositide metabolism, cytocolic calcium levels, cGMP levels, PKC, MAP kinases and the opening of chloride channels [9, 12]. Although animal experiments have shown that $1,25(OH)_2D_3$ can induce immediate responses in several different cell types, the pathways to which these responses occur remains to be identified [4].

Classic functions of vitamin D

Vitamin D is essential for promoting calcium absorption in the gut and maintaining adequate serum calcium and phosphate concentrations to enable normal mineralisation of bone and also to prevent hypocalcemic tetany [4]. For this reason, rickets in children and osteomalacia in adults are clinical manifestations of vitamin D deficiency [13]. Furthermore, it is needed for bone remodelling, and protects against osteoporosis in older adults [14].

Together with parathyroid hormone (PTH) vitamin D keep calcium levels in serum constant by three mechanisms. Firstly, vitamin D induces transcription of genes that are involved in active intestinal calcium absorption. Secondly, vitamin D mobilises calcium from bones when calcium is not available from the gut. Thirdly, vitamin D stimulates the kidneys (distal renal tubule) to reabsorb 1% of the filtered load of calcium (7 g of calcium are filtered through the kidneys everyday) [2].

When serum levels of calcium decline, it stimulates the production and secretion of PTH from the parathyroid gland. PTH then stimulates 1α-hydroxylase in the kidney which in turn increases the production of $1,25(OH)_2D_3$. $1,25(OH)_2D_3$ then increase the calcium concentrations by the three aforementioned mechanisms. $1,25(OH)_2D_3$ inhibits PTH synthesis and parathyroid cell growth via direct transrepression of the PTH gene by the $1,25(OH)_2D_3$-VDR complex [4].

Non-classic functions of vitamin D

In more recent years, it has been well established that vitamin D is important for diseases that are not related to calcium homeostasis. Wang published a review that focused on ecological, case-control and cohort studies where the role of vitamin D in health and disease were explored. Of disorders not related to calcium homeostasis they highlighted the possible function of vitamin D in muscles, autoimmune diseases, type 2 diabetes, cardiovascular diseases and cancer [1]. Furthermore, the understanding of the underlying mechanisms in which vitamin D exerts its effects on these diseases is growing with an increasing body of evidence [4].

1.2 Vitamin D and the elderly

1.2.1 Recommendations

Requirement of a nutrient is the lowest amount needed to avoid clinical symptoms while recommended intake includes a security margin to account for individual variability and uncertainties in the data [15]. Generally, the unfavourable effects of low plasma 25(OH)D begin to accumulate at levels below 50 nmol/L, although some studies have suggested higher threshold levels. Lips et al proposed that levels below 50 nmol/L should be defined as insufficiency, levels below 25 nmol/L should exemplify deficiency and levels below 12 nmol/L should be characterised as severe deficiency [16]. Levels between 25 and 12 nmol/L may cause proximal myopathy or increased bone turnover, whereas levels below 12 nmol/L are frequently present in individuals with rickets and osteomalacia [17].

The different threshold levels used by different researchers make the use of the words “deficiency” and “insufficiency” somewhat arbitrary. In the present thesis the terms “insufficiency” and “deficiency” are defined according to Lips’ previously mentioned suggestion unless otherwise stated.

To ensure an acceptable vitamin D status in the population, the recommended dietary intake of vitamin D according to the Nordic Nutrition Recommendations 2004 is 10

µg/d for the age groups 6-23 months and above 61 years and 7.5 µg/d for all other age groups (**Table 1**) [18].

Table 1. Nordic recommendations according to sex and age groups

	Vitamin D (µg/d)		
Age	**Children**	**Men**	**Women**
6 - 23 months	10		
2 - 9 years	7.5		
10 - 60 years		7.5	7.5*
≥ 61 years		10	10

* 10 µg for lactating and pregnant women

Compared to the previous edition of NNR, the recommendation for the age groups 2–60 years has been increased by 50% from 5 µg/d to 7.5 µg/d; this is in order to diminish the seasonal drop in plasma 25(OH)D during the winter months [15].

1.2.2 Vitamin D status and intake

The prevalence of vitamin D deficiency is high in the elderly population [16], and it has been estimated that 40-90% of the elderly worldwide have vitamin D insufficiency (≤75 nmol/L) [19].

Lips et al report that vitamin D insufficiency is a common finding among community-dwelling elderly, and almost an exclusive finding among institutionalized elderly [16, 17]. In the USA however, vitamin D status amongst the elderly is more acceptable, probably a result of liberal fortification politics [20].

The Nordic countries cover latitudes from approximately 54° N in Denmark to 72° in northern Norway [21]. It has been reported that people living in high latitudes often have a reduced endogenous production of vitamin D as the UV wavelengths are less than optimal for dermal production of the vitamin [22]. An adequate intake to compensate for this issue is therefore of particular relevance to populations in the Nordic countries.

In Denmark, 80% of elderly over 65 years had vitamin D insufficiency and 44% of nursing home residents had severe vitamin D deficiency [23]. Mosekilde et al found

that there was a strong seasonal variation in serum 25(OH)D in a Danish population. The results showed a marked downward shift during the winter months, with levels falling well below desirable vitamin D status in a large part of the population [23]. Lips et al found however that within Europe, serum 25(OH)D was positively related to latitude, contrary to what would be expected [16]. The highest serum 25(OH)D levels were observed in Scandinavian countries and the lowest levels were found in Southern Europe. They speculate that this may be due to high sun exposure, a light skin and multivitamin use in northern countries while shadow-seeking behaviour and a darker skin tone are more common in Mediterranean countries [16].

A study from Finland showed that participants had a satisfactory vitamin D status during summer, whereas a large portion of the subjects had a poor vitamin D status during the months of winter [24]. More adequate serum levels of 25(OH)D were found in a similar study from Tromsø [25]. One explanation for the disparity observed in vitamin D status between the two population groups during the winter months is that, at the time of these studies, the intake of fish/fish products and margarine fortified with vitamin D was a lot higher in Norway than in Finland [15].

Data from the National Nutrition Council from 2006 indicate that the intake for the elderly population in Norway is very low compared to the recommended intake (**Table 2**) [15, 26]. Furthermore, it appears as though supplementation is very important for the total intake of vitamin D.

Table 2. Intake of vitamin D according to a Norwegian nationwide survey (Norkost 1997)

Age group	n	Vitamin D without supplemntation (µg/d)[1]	Vitamin D with supplementation (µg/d)	Below recommended intake (%)
60 - 79 years				
Women	246	4.0 (2.2)	12.5 (10.8)	47
Men	237	5.8 (3.8)	13.9 (11.0)	48

[1] Mean (SD). All such values

1.2.3 Challenges

The elderly population is at increased risk of developing vitamin D deficiency for a number of reasons. Both biological and behavioural issues make this population particularly vulnerable. Such factors can be disadvantageous on their own or, more expectedly synergistic.

The biological factors that contribute to the increased risk of a poor vitamin D status in the elderly are a reduced capacity to synthesise the vitamin in the skin, in addition to a decrease in the renal production of $1,25(OH)_2D_3$ as a result of diminishing renal function with age [27, 28]. Holick et al found a >4-fold difference in elevation of serum cholecalciferol level induced by standard skin exposure to UVB radiation in individuals aged 62-80, as compared to 20-30 year old controls [29].

Behavioural factors that add to the risk of having a poor vitamin D status in the elderly population are many. They are, however, easily modifiable (at least in theory). Elderly that are institutionalised have been shown to have a very poor vitamin D status, a result of getting little, if any, exposure to sunlight [29]. Another factor related to sunlight exposure is that elderly usually cover themselves up more than adolescents [30]. The use of sunscreens and the fact that the larger part of the modern population work indoors during the hours when the dermal production of vitamin D in response to solar radiation is at its maximum, contribute to the reduced production of vitamin D in the skin [30].

1.3 Vitamin D and Cognition

Dementia is the progressive decline in cognitive function due to the presence of disease or damage in the brain [31]. The pathology of dementia is complex and may involve a number of mechanisms including oxidation, inflammation, disease induced neurotoxicity, and genetic vulnerability [32-34]. Alzheimer's type dementia and vascular dementia are the most common forms of age-associated dementia [32]. Ferri

et al reviewed evidence from epidemiological studies and estimated that 24.3 million people have dementia today, with 4.6 million new cases of dementia every year (one new case every 7 seconds). They go on to say that the number of people affected will double every 20 years to 81.1 million by 2040 [35]. Alzheimer's disease is the sixth leading cause of all deaths in the United States [36].

1.3.1 Clinical evidence

Several studies have shown an association with Vitamin D in serum and cognitive decline [37-40]. These, however, are observational studies, and so far evidence based on randomized clinical trials is lacking. Furthermore, several studies have found no relationship between serum vitamin D concentrations and cognition [41, 42]. A review article by Annweiler et al reviewed 5 cross-sectional studies that had looked into the relationship between serum 25(OH)D and cognition found the evidence to be inconclusive [43].

The biological plausibility for an association between vitamin D and cognition is however well supported [44].

1.3.2 Biological evidence

VDR polymorphisms

The vitamin D receptor (VDR) is highly expressed in regions of the brain that is affected in conditions that is related to cognitive impairment [45]. The VDR gene contains several polymorphisms of which five; *Cdx-2*, *FokI*, *BsmI*, *ApaI* and *TaqI*, have been most frequently investigated [46]. These have been associated with a number of phenotypes, such as bone mineral density, and risks for fractures and cancer [11]. In addition, haplotype alleles have been identified that influence the risk of osteoporotic fractures and the expression of the VDR gene [47, 48]. The risk haplotypes that have recently emerged, *baT* and *BAt*, are composed of the *BsmI*, *ApaI* and *TaqI* polymorphisms [46].

It has been shown that animals exposed to prenatal vitamin D deficiency have alterations in brain morphology [49], locomotion [50], and learning and memory [51]. In addition, mice lacking a functional VDR gene appear to suffer from anxiety-like behaviour [52, 53].

Kuningas et al concluded that genetic variance in the VDR gene influences the susceptibility to age-related changes in cognitive functioning and in depressive symptoms [46]. The study was carried out in the prospective population-based Leiden 85-plus Study. Participants of the study were genotyped for *Cdx-2*, *FokI*, *BsmI*, *ApaI* and *TaqI* polymorphisms in the VDR gene. The data revealed an overall worse performance on tests measuring cognitive functioning for carriers of *BsmI* and *TaqI* polymorphisms, and of haplotype *BAt*. In contrast, carriers of *ApaI* variant-allele and of haplotype *baT* had better cognitive functioning together with less depressive symptoms. Furthermore, they make a point of saying that the associations discovered in the study could not be explained by differences in calcium levels or by selective survival, since no associations between the VDR gene variants and calcium levels and mortality were observed [46].

Neuronal protection

Studies have shown that protection of the structure and integrity of neurons through detoxification pathways as well as neurotrophin synthesis are both processes in which vitamin D is involved [54-58].

The enzyme inducible nitric oxide synthase (iNOS) is inhibited by $1,25(OH)_2D_3$. This enzyme is up-regulated during ischemic events and in patients with Alzheimer's disease [59].

$1,25(OH)_2D_3$ boost innate antioxidant pathways. Gamma glutamyl transpeptidase is up-regulated by the active hormone which consequently leads to an increase in glutathione [60]. Glutathione is an innate antioxidant which protects oligodendrocytes and the nerve conduction pathway vital to mental processing [31].

Neurotrophins (NT) are proteins necessary for neuronal survival in aging and neuropathological conditions [61]. When neurotrophin synthesis is decreased, spatial navigation is compromised [61]. $1,25(OH)_2D_3$ up-regulates protective neurotrophin factors, such as neurotrophin-3 (NT-3) and glial cell line derived neurotrophic factor (GDNF) [54, 55]. NT-3 protects nerve transmission and synapticity [56-58] [61]. GDNF affects the survival and differentiation of dopaminergic cells [31].

Co-localisation of VDR and $1,25(OH)_2D_3$ in the brain

Evidence supporting a ligand mediated VDR pathway in the human brain is a recent finding.

An early study of patients with Alzheimer's disease revealed the presence of *VDR* mRNA in humans [62], yet the presence and accessibility of $1,25(OH)_2D_3$, necessary for activation of the nuclear pathway, remained unclear [31].

Neuronal and glial cells, cerebral purkinje cells and cells in the cerebral cortex are particularly vulnerable to age and degeneration related to disease [31]. Biosynthetic and degradative pathways for $1,25(OH)_2D_3$ have been discovered in the abovementioned cell types [54, 55, 63, 64].

A study of human brains confirmed the presence of the VDR as well as genes encoding catalytic enzymes in $1,25(OH)_2D_3$ metabolism in both neuronal and glial cells within brain structures critical for cognition [45, 50, 64]. Furthermore, the VDR and catalytic enzymes were co-localized in the brain. These findings support a functional role for vitamin D in the human brain [31].

1.3.3 Vitamin D in relation to dementias

Vascular dementia

Vitamin D may help improve vascular-related brain disease by attenuating damaging effects of calcium dysregulation, increased oxidative stress and inflammation [44].

Hippocampal cell loss and neuronal ageing, both of which are important in neurodegenerative diseases, have been attributed to elevated L-type voltage calcium channel density and glucocorticoid neurotoxicity [65]. Studies have shown that vitamin D mediate regulatory benefits in neuronal calcium homeostasis and protects neurons from excess calcium entry in the brain [66]. These beneficial changes protect brain neurons during ischemic events.

Neurotrophins are proteins necessary for neuronal survival in aging and neuropathological conditions [61]. $1,25(OH)_2D_3$ up-regulates protective neurotrophin factors, such as neurotrophin-3 and glial cell line derived neurotrophic factor [54, 55]. Both up-regulation of glial cell line derived neurotrophic factor and the increase in innate antioxidative defences have been shown to attenuate ischemic brain disease in rodents [67].

Vascular related brain damage may result from inflammatory responses. Vitamin D inhibits antigen-presenting cell maturation, down regulates NF-κB and stimulates anti-inflammatory cytokine production [68-70], and so acts as an anti-inflammatory agent. Epidemiological studies have found an inverse relationship between vitamin D and C-reactive protein levels, a marker of inflammation [70].

Vitamin D may play a role in protection against cardiovascular and cerebrovascular disease [71-73]. Intervention with vitamin D has been shown to regulate blood pressure, cardiac hypertrophy, and plasma renin activity [74-78]. It is reasonable to believe that vitamin D may influence vascular-related dementia via these indirect mechanisms [31, 44].

Alzheimer's disease

Hippocampal neuronal loss is a characteristic finding in Alzheimer's disease. Treatment with $1,25(OH)_2D_3$ attenuated hippocampal atrophy and protected neuron density in aging rats [79].

Data in human subjects with Alzheimer's disease revealed a reduction in VDR mRNA in specific regions of the hippocampus compared to controls [62] and a higher

frequency of VDR polymorphisms were found in Alzheimer's brains than in age-matched controls [80].

Table 3 summarises the mechanisms whereby vitamin D metabolites may protect the brain.

Table 3. Mechanisms whereby vitamin D metabolites may protect the brain

Factor	Mechanism
Neuronal protection	Inhibition of iNOS Enhances antioxidant pathways. Upregulates neurotrophin factors.
Neronal calcium regulation	Protects against excess calcium entry into the brain.
Reduction of inflammatory factors	Inhibits antigen presenting cell maturation Down regulates NF-κB Stimulates anti-inflammatory cytokine production
Vasculoprotection	Regulates blood pressure Regulates of cardiac hypertrophy Regulates plasma renin activity

Adapted from W.B. Grant 2009 Does Vitamin D reduce the Risk of Dementia?

1.4 Rationale of the thesis

As the population's lifespan increase, so does the prevalence of different dementias and cognitive deficits. It is of great interest to find preventative strategies for this disease to relieve both the financial burden on society, and the emotional burden experienced by the patient and his or her surrounding family.

In the January issue of Neurology 2010, it was stated in the editorial that "… *more research (in regards to vitamin D and cognition) needs to be performed in both men and women living in the community (…) Patients with vitamin D deficiency should be given more cognitive testing to see which aspects of their thinking are affected.*"

2. Objectives

Elderly are at particular risk for developing vitamin D deficiency. The present study focuses on the intake of vitamin D in relation to cognition in older subjects using data from the Hordaland Health Study, a population with a high intake of fish and fish oils. The objective was to examine the cross-sectional relationship between intake of vitamin D and cognitive performance.

The specific aims of the study were:

To describe the sources of vitamin D in the study population

To investigate the effect of cod liver oil on intake of vitamin D in the study population

To study the association between intake of vitamin D and cognitive function, including poor cognitive function in the study population

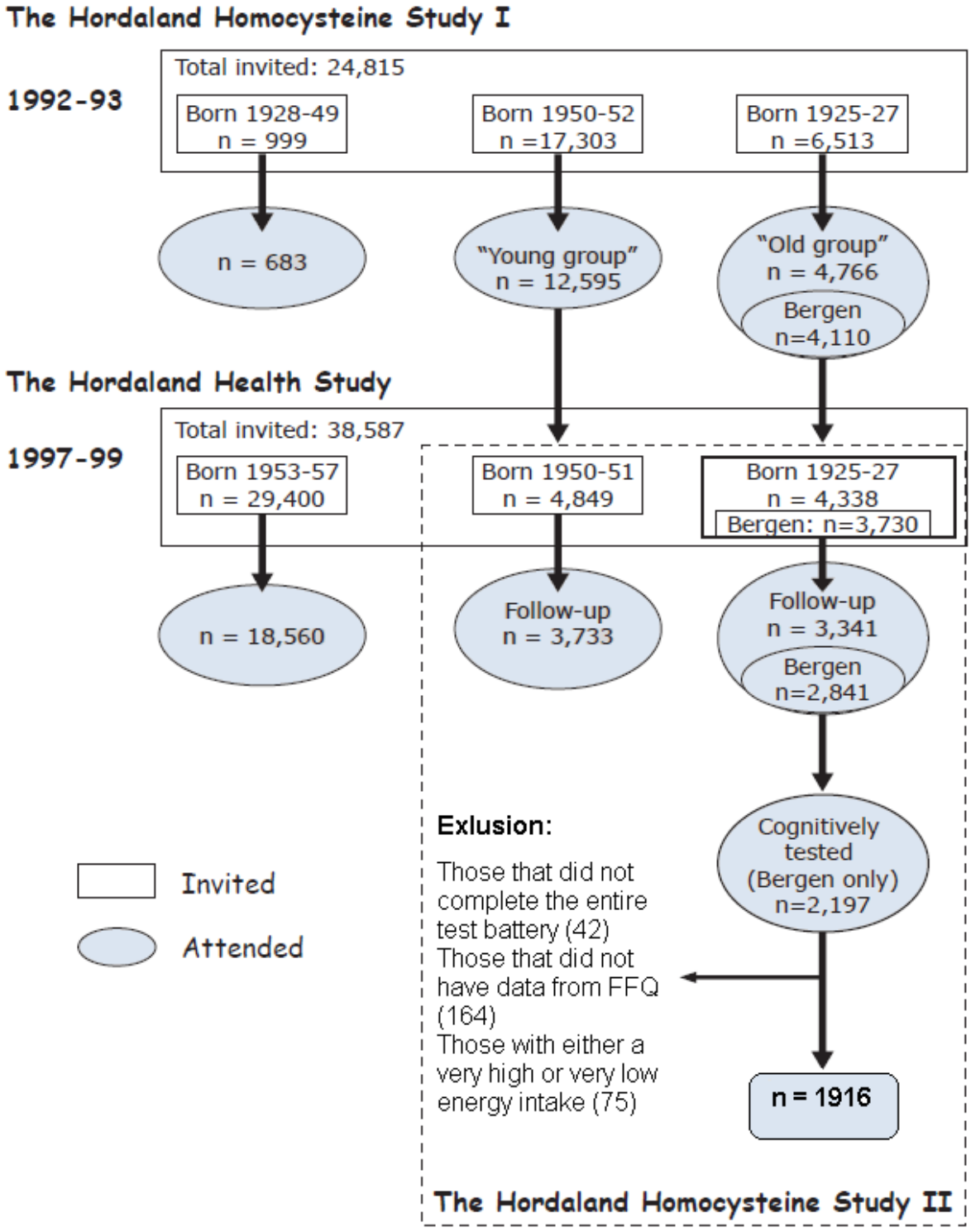
To study the intake of cod liver oil, lean fish and fatty fish in relation to cognition in the study population

3. Study population and methods

3.1 Study population

The baseline examination of the Hordaland Homocysteine Study (HHS) was conducted in the Hordaland County of Western Norway from April 1992 to April 1993 as a collaboration between the national health screening service, local health services and the University of Bergen. The eligible subjects were selected from the national population registry, identified by place and residence and age on December 31, 1992. A total of 24 815 subjects from three age groups were invited. The youngest age group included all subjects in the county who were born in 1950, 1951 or 1952 (40-42 years of age at the time of data collection). The older age group covered all subjects born in 1925, 1926 and 1927 (65-67 years at the time of data collection) residing in Bergen and three neighbouring suburban municipalities. A third group born between 1925 and 1949 (43-65 years) was a 2% random sample of residents in Bergen. The overall attendance rate was 72.7% (N = 18 044). In the Hordaland Health study (HUSK), performed in 1997-99, a selection of the youngest age group and all of the living participants of the older age group were re-invited. A total of 9187 individuals were re-invited, and the overall attendance rate was 77.0 % (N = 7074). The number of elderly re-invited in HUSK to examine age effects was 4338 in which 3341 took part in the study. Recruitment into the Cognitive Substudy is described on the Web (Internet: www.uib.no/isf/husk/Vedlegg_dokumenter/Cognitive_Sub_study.pdf). A total of 2155 subjects completed the cognitive test battery. Of those, 1991 individuals completed a food-frequency questionnaire. Participants with a very low energy intake (< 3000 kJ for women < 3300 for men), or very high energy intake (≥ 15000 kJ for women; ≥ 17500) for men were excluded from the analyses (Berstad, Konstantinova et al. 2007), leaving a total of 1916 subjects in this study on cognition and vitamin D intake. All participating subjects gave their written informed consent (Appendix I). The study protocol was approved by the Regional Committee for Medical Research Ethics of Western Norway. Recruitment in HHS and HUSK is depicted in **Fig 1**.

Figure 1. Recruitment in HHS and HUSK



3.2 Data collection

The study included three self-administered questionnaires, two of which are relevant to the present thesis. Briefly, the main 4-page questionnaire (Appendix II) used by the National Health Screening Service was sent together with the invitation letter (Appendix III), filled out at home, collected and checked for errors by a nurse at the examination day. Information included parity, physical activity, smoking, consumption of coffee and alcohol, education as well as current use of prescription and over-the-counter medications. Usual dietary habits during the last year were assessed by a comprehensive 169-item food frequency questionnaire (FFQ) (Appendix IV). The questionnaire was developed at the section for dietary research, Department of Nutrition research at the University of Oslo. It was handed out at the examination day, filled out at home and mailed to the HUSK project centre in Bergen.

Cognitive testing was performed at the study location by trained nurses after the standard cardiovascular examinations of the National Health Screening Service were completed. The cognitive test battery included 6 tests (Appendix V).

Baseline measurements included height, weight, waist and hip circumference, blood pressure, heart rate, non-fasting analyses of serum total cholesterol, HDL-cholesterol, triglycerides, and glucose. Nonfasting EDTA blood samples was collected for the measurement of total homocysteine (tHcy), related B vitamins, creatinine and gene polymorphisms.

3.2.1 Dietary habits

The intake of vitamin D was self-reported and estimated using data from an FFQ. The FFQ has been validated by several studies [81-85].

The FFQ included 169 food items that were grouped according to Norwegian meal patterns. It was designed to obtain information on usual food intake during the past year. The frequency of consumption was given per day, week, or month. The portion sizes were given as household measures, or units such as slices or pieces. In addition to

food groups the questionnaire also included questions about dietary supplement intake, in which the product names of the most used supplements in Norway were considered. The subjects were advised to estimate an “average” of amounts of food.

The intake of vitamin D per person according to food group was calculated by the use of a food database and software system developed at the Department of Nutrition, University of Oslo (Kostberegningssystem, KBS, version 3.2; University of Oslo, Oslo, Norway) [82].

Fish and fish products, supplements, butter and margarines, eggs and dairy products are sources that contribute to the total vitamin D intake in the Norwegian population. Butter and margarines as well as some dairy products are fortified with vitamin D. Fish and fish products were reported as dinner dishes or bread spreads (sandwich fillers). Dinner items were reported as how many times the food item was consumed per month and amount of food per consumption. Entities differed according to food item depending on what was appropriate for the specific food in question (e.g. piece, fillet, dL etc). The items in the fish category were fishcakes, fish pudding or fish balls, fish fingers, cod, coalfish, or haddock (either poached or fried), mackerel, salmon, trout, fish stew/soup/gratin, or shrimp/crab. As bread spreads the amount of food item was reported as number of slices of bread needed for the amount of bread spread pr week. The food items were caviar, mackerel in tomato paste/smoked mackerel, sardines/pickled herring/anchovies, salmon/trout and shrimp/crab. Use of supplements was reported as “seasonal use” (during the whole year or only winter half of the year), frequency per week, and amount per time. Eggs were reported as how many eggs per week. Types of egg dishes included boiled, fried, scrambled or as an omelette. Dairy products that contain vitamin D was recorded as milk as a drink with amounts as number of glasses per day, and for cheese as bread spreads as well as cheese on pizza. There are three questions regarding the use of butter and margarine including the use of these products as a bread spread, use in cooking in general, and as a dinner supplement. In the question dealing with fat as a bread spread it was asked what product was preferred, and if it was used both in the weekdays and the weekend. There was also a question that asks how many slices of bread a 12 g pack of butter would last

to get an impression of the amount the individual was using. In the “cooking in general” question it was asked which product was preferred, but there was no question regarding the amount. As a dinner supplement melted butter/margarine was an option. Amount was given in table spoons.

The calculated intake of vitamin D from the individual food groups showed that cakes and cookies, potato and vegetables had limited amounts of vitamin D. Cakes and cookies had vitamin D from butter/margarines, as did potatoes (french fries) and vegetables (fried onions). These variables were for that reason added to the butter/margarines group. The food group “Cereals” include flour, rice pasta, pizza and breakfast cereals and had small amounts of vitamin D from the pizza group that contains cheese. Vitamin D from “Cereals” was therefore added to the “Dairy products” variable. The food groups “Fruit” and “Juice” were also added together. The combining of variables did not change the results in the final analyses.

3.2.2 Cognitive tests

In the present study, the following cognitive tests were used: The abridged version of the Controlled Oral Word Association test (S-task), the Kendrick Object Learning test (KOLT), the modified version of the Digit Symbol Test (m-DST), the Trail Making Test Part A (TMT-A), the modified version of the Block Design test (m-BD), and the modified version of the Mini Mental State Examination (m-MMSE) which is a global cognitive test. A sum Z-score variable was calculated by adding together the Z-scores from all the cognitive tests with the exception of the m-MMSE. The sum Z-score represents global cognition, but unlike the m-MMSE has the advantage of being normally distributed, without ceiling effect.

The Controlled Oral Word Association Test

The controlled oral word association test is a test of verbal fluency (access to semantic memory and psychomotor speed) consisting of three word naming trials. The set of letters that was first employed, FAS, has been used so extensively that this test is sometimes called FAS [86]. Words beginning with the first letter of the set have a

relatively high frequency. The second letter has a somewhat lower frequency, and the third letter has a still lower frequency. To give the test, the examiner asks subjects to say as many words as they can think of that begin with the given letter of the alphabet, excluding proper nouns, numbers, and the same word with a different suffix. The score is set as the sum of all acceptable words produced in a one minute trial. In the abridged version (S-task) of the Controlled Oral Word Association Test [87], the subjects were required to generate as many words as possible beginning with the letter *S* within 60 seconds [88].

Kendrick Object Learning Test

The Kendrick Object Learning Test (KOLT) is commonly used in Norway and is designed to assess dementia status and memory performance among non-institutionalized elderly [89]. The KOLT has been validated for the detection of memory impairment in old age [90]. Four cards with 10, 15, 20 and 25 pictures are shown individually for 30, 45, 60 and 75 seconds. When each card is taken away, the subject is asked to name as many pictures on the card as he or she can remember. A possible maximum KOLT score is 70. A score of 20 or less is categorized as severely memory impaired or demented, whereas a score of 21 to 25 is considered moderately memory impaired. The KOLT is of great value to community studies because it is normally distributed, and thus does not show a ceiling effect [91].

The Digit Symbol Test

The digit symbol test consists of four rows containing in all 100 small blank squares, each paired with a randomly assigned number from one to nine. Above these rows is a printed key that pairs each number with a different nonsense symbol. Following a practice trial on the first ten or seven squares, the task is to fill in the blank spaces with the symbol that is paired to the number above the blank space as quickly as possible for 90 seconds. The score is the number of squares filled in correctly. For most adults Digit Symbol is a test of psychomotor performance that is relatively unaffected by intellectual prowess, memory, or learning [86]. The modified version of the Digit Symbol Test [92] is regarded as a measure of focused attention, visuomotor

coordination, and psychomotor speed. In the present version, the number of correct matches between digits and symbols in 30 seconds was recorded [88].

Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) covers various aspects of cognitive function, including orientation to time and place, naming, repeating, writing, copying, instantaneous recall, short-term memory, backward spelling, and performing a 3-stage command [93]. This formalized mental status examination is probably the most widely used brief screening instrument for dementia used either alone or as a component in a test battery. It tests a restricted set of cognitive functions. Administration takes from five to ten minutes. The standardized administration and scoring procedures are easily learned. Scores below 24 are considered abnormal for dementia and delirium screening, but higher cut-off scores have been recommended for specific conditions. The modified version of the Mini Mental State Examination (m-MMSE) consists of 12 of the 20 items in the full version of the MMSE and has been shown to be just as effective as the full version when the purpose is to identify elderly subjects with cognitive impairment [94].

Trail Making Test

The trail making test is originally given in two parts, A and B. The subject must first draw lines to connect consecutively numbered circles on a work-sheet (Part A) and then connect the same number consecutively numbered and lettered circles on another worksheet by alternating between the two sequences (Part B). The subject is urged to connect the circles as fast as he/she can without lifting the pencil from the paper [86]. Reitan introduced the scoring method used in this study and is the most common one today [95]. The Trail Making Test, part A (TMT-A) is a test of visual conceptual and visuomotor tracking, involving motor speed and attention functions. The score is the total time in seconds to complete the items [88].

Block Design

The Block Design tests visuospatial and motor skills [86]. The Block Design test is a construction test in which the subject is presented with red and white blocks, four or nine, depending on the item. Each block has two white and two red sides, and two half-red half-white sides with the colours divided along the diagonal. The task is to use the blocks to construct replicas of two block constructions made by the examiner and eight designs printed in smaller scale. The order of presentation differs in the order of difficulty. Generally, at each level of complexity, the even-numbered items are likely to be more difficult than the odd-numbered items. The short form (m-BD), used in the present study, included 4 of the 10 patterns presented in the original test (patterns 1, 2, 5, and 6). Every correct matching gives 4 points; thus, a possible maximum score on the m-BD short form is 16 [88]. The test is normally discontinued after three failures. Block Design lends itself well to qualitative evaluation. The manner in which patients work at Block Design can reveal a great deal about their thinking processes, work habits, temperament, and attitudes toward themselves [86].

3.2.3 Other variables

Serum concentrations of lipid-related factors, glucose and creatinine were measured at Ullevål hospital (Department of Clinical Chemistry) using a Hitachi 911 analyzer for the whole study. This analyzer comes with adapted reagents and measure methods from the company Boehringer Mannheim FRG (now: Roche, Basel, Switzerland). See also article in Norsk Epidemiologi 2003;13(1):85-88 (Norwegian):

http://www.ub.ntnu.no/journals/norepid/2003-1/2003(1)Foss.pdf

Nonfasting EDTA blood samples were collected for the measurement of total homocysteine (tHcy), creatinine and gene polymorphisms. The EDTA sample was kept cool until centrifuged. The blood samples were stored at -80 degrees C. The duration of storage ranged from a few days to 18 months. Plasma tHcy was measured by using a fully-automated HPLC assay [96, 97]. Apolipoprotein E (ApoE) genotypes were

determined in the packed cell fraction of blood samples by using a one-stage polymerase chain reaction method [98].

A history of cardiovascular disease (CVD) was defined as self-reported information at baseline, or during follow-up from 1992-1998. On the basis of information from both surveys, the subjects were categorized as with or without a history of CVD (myocardial infarction, angina pectoris, stroke, thrombosis, phlebitis, and hypertension). A history of diabetes was self-reported [88].

Educational level was self-reported and recorded in 6 categories: Not completed primary school, primary school (9 years), technical college (10-12 years), secondary school (10-12 years), and college or university less than 4 years and more than four years.

The follow-up study in 1997-99 included assessment of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) which consists of two 7-item subscales, HADS-A for anxiety and HADS-D for depression [99, 100]. HADS-A contains items mainly related to restlessness and worry, and one item reflects panic attacks. HADS-D focuses mainly on the reduced pleasure response aspect (anhedonia) of depression, but it also includes psychomotor retardation and impaired mood. In this study, only the HADS-D score was used as it is more relevant to cognitive function [101]. When tested, HADS-A was not associated with vitamin D.

The smoking variable is coded as number of cigarettes smoked per day.

Blood pressure was measured three times and the variable used in this study is the average of the second and third measurements.

3.3 Statistical Analyses

All calculations were performed by using SPSS 16.0 (SPSS INC, Chicago IL). Results are expressed as medians with 25^{th} and 75^{th} percentiles or means with standard deviations (SD). Pearson's chi-square test and Student's *t*-test were used to examine

relationships between independent groups. Univariate ANOVA was used to compare the effectiveness of taking cod liver oil on total vitamin D intake. Spearman's rho correlation coefficients were used to assess simple correlations. Multiple linear and logistic regression analyses were performed to examine relationships between intake of vitamin D (entered as quintiles) and the cognitive test scores adjusted for relevant covariates. In the logistic regression analyses, the categories of intake were chosen to examine whether a low intake would increase the risk of scoring poorly on a cognitive test using the highest quintile as reference (vitamin D intake ≥15.7µg/d). A poor cognitive test score was set to the ~10^{th} percentile for all the tests, except for the TMT-A, where the 90^{th} percentile was used [88, 102]. To avoid over-adjustment, three regression models were routinely used; first adjusting for sex only, then two with multiple adjustments. When adjusting for potential confounders, it was decided to adjust only for well established determinants of cognitive function (e.g. education, ApoE variant *ε4* allele status) or for variables that were significantly associated with 4 or more of the cognitive tests (including sum Z-score) as well as vitamin D intake. In the second model, the following variables were included: sex (men or women), education (6 categories), ApoE *ε4*variant allele (presence or not presence of *ε4* variant allele), tHcy (quintiles), and total energy intake (quintiles). The third model also included nutritional covariates (quintiles) in addition to the aforementioned variables. Consequently, this model adjusted for sex, ApoE variant *ε4* allele, education, tHcy, total energy intake, cereals, meat and meat products, fruit, vegetables, sweets, tea and wine. Month of cognitive testing in relation to the cognitive scores was assessed. For several of the tests, the lowest scores obtained were in August and September. However, adjusting for this variable did not change the results and it has been omitted from the final analyses.

Because the subjects in this sub-study are homogenous in age, age is not included as a cofactor in the statistical models.

It was chosen to enter continuous adjustment variables as quintiles in the regression models. Thus, log-transformation and the use of geometric means could be avoided.

Cod liver oil is an important source of vitamin D in the present population. Multivariate linear regression analysis was used to investigate whether intake of cod liver oil was associated with KOLT score. Three regression models were used, where the two first models were as previously described. The third model adjusted for other vitamin D containing sources in addition to the variables in model 2. The third model therefore included sex, ApoE variant *ε4* allele, education, tHcy, total energy intake, fatty fish, lean fish, fish remaining, butter/margarines, dairy products, eggs and other kinds of supplements. Again, all continuous variables were entered as quintiles.

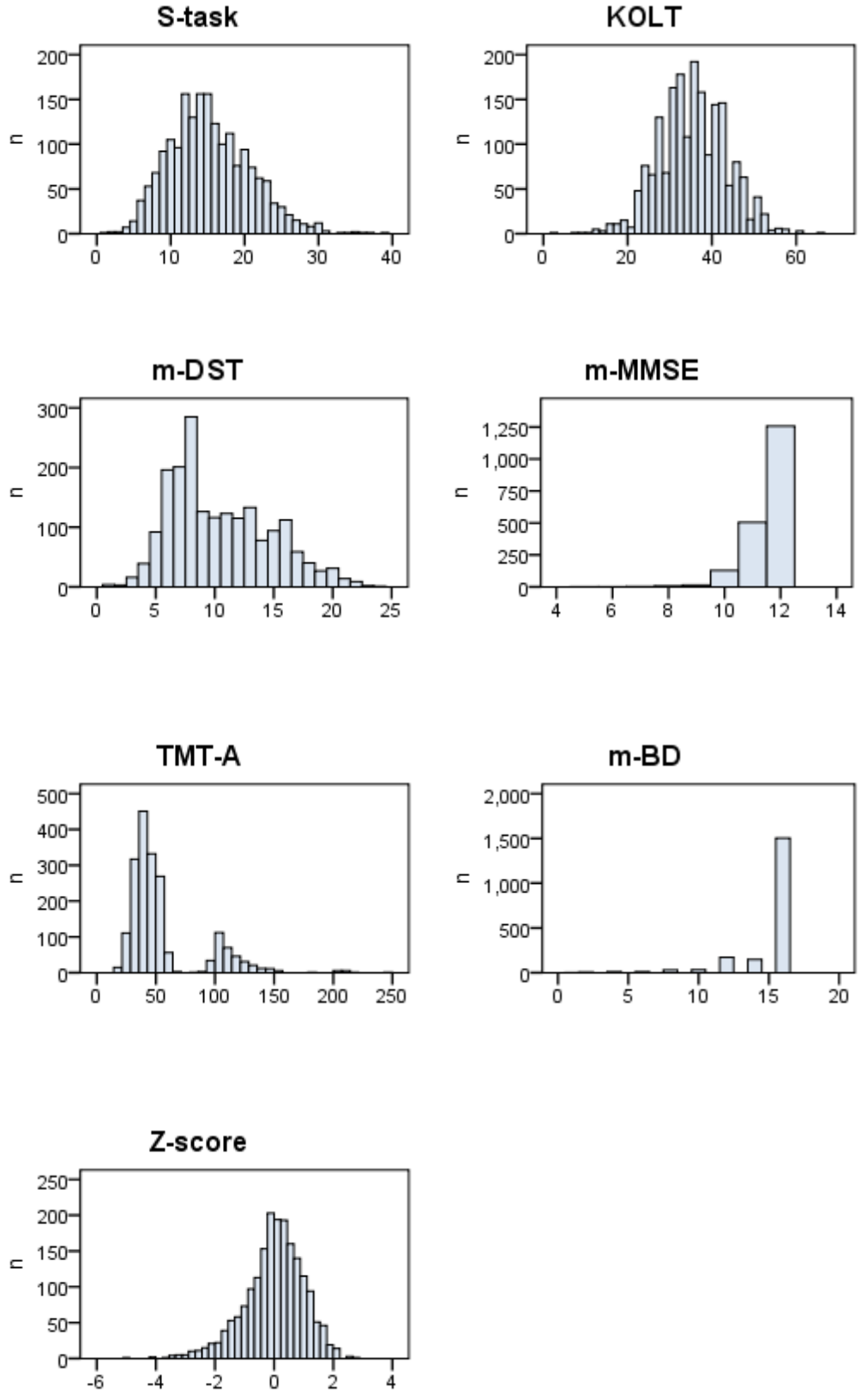
Binary logistic regression analysis was performed to examine if intake of lean fish and fatty fish affected the risk of scoring poorly on the KOLT differently in users/non-users of cod liver oil. KOLT score was entered as dependent variable (dichotomous, 10^{th} percentile as cut-off) and intake of lean fish (4 categories: 0, 0.1 – 25.0, 25.1 – 50.0 and ≥50.1 g/d) and fatty fish (4 categories: 0.0, 0.1 – 10.0, 10.1 – 20.0 and ≥20.1 g/d) was entered as indicator variables. For both types of fish the highest intake group was used as reference. In addition to adjust for lean fish and fatty fish mutually, we also adjusted for sex, education, ApoE ε4 variant allele, tHcy and total energy intake. Also, a model was created that adjusted for other important sources of vitamin D (butter/margarine and other types of fish, dairy products, eggs and the remaining supplements, in quintiles). Finally, the same analysis was also conducted by entering cod liver oil as an adjustment variable instead of selection variable (3 categories: 0, 0.1 – 2.5, ≥2.6 g/d).

The distributions of the different tests varied greatly, and whereas the S-task, KOLT, m-DST and Z-scores were more or less normally distributed, the distributions of the m-MMSE, TMT-A and m-BD were markedly skewed (**Fig 2**). The tests differ in nature, and the m-MMSE, TMT-A have a ceiling effect. In addition, the TMT-A has a rather untraditional appearance. The histogram (Fig 2) suggests that it is a clear divide within the population. We have not been able to map out what could be the reason for such a pattern, but have speculated that there is a discrepancy perhaps in the execution of the test. Even though some of the data were not normally distributed, it was chosen to analyse them using linear regression analyses as the sample size is very large [103].

For some of these tests, logistic regression analyses obviously appear to be more appropriate.

All P-values are 2-sided, and values < 0.05 were considered significant.

Fig 2. Histograms showing the distributions of the different cognitive tests

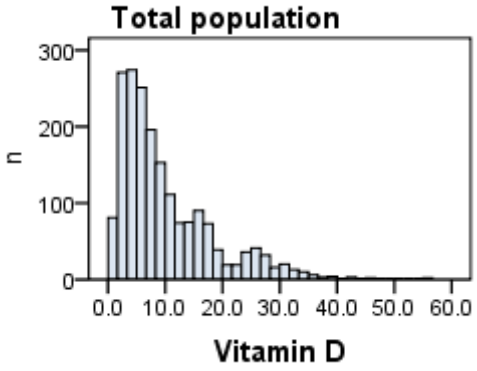


4. Results

4.1 Dietary intake

The intake of vitamin D in the present population ranged from 0.5 to 56.1 µg/d. The distribution of vitamin D intake in the total population is depicted in **Figure 3**.

Figure 3. Distribution of Vitamin D intake in the total population



In the total population, intake of fish and fish products was the most important food group with fatty fish as the source that provided the most vitamin D (**Table 4**). Butter/margarines were the second most important source of vitamin D, followed by supplement use. Within the supplement category, cod liver oil was the strongest provider of vitamin D. Eggs and dairy products have small amounts of vitamin D in them and contributed modestly to the total intake of vitamin D.

Table 4. Sources of vitamin D, the mean contribution of each source, and intake of the food group in the total population

	Total population (n = 1916)		
	Mean[1]	Median[2]	Contribution[3]
Supplements total			
Total intake (g/d)	2.1 (3.5)	0.0 (0.0, 2.8)	
Vitamin D (µg/d)	4.2 (7.1)	0.0 (0.0, 6.05)	23.4 (31.3)
Cod liver oil			
Total intake (g/d)	1.7 (3.0)	0.0 (0.0, 2.0)	
Vitamin D (µg/d)	3.6 (6.5)	0.0 (0.0, 4.3)	18.8 (29.1)
Supplements remaining			
Total intake (g/d)	0.4 (1.6)	0.0 (0.0, 0.0)	
Vitamin D (µg/d)	0.6 (2.1)	0.0 (0.0, 0.0)	4.6 (13.9)
Fish total			
Food intake (g/d)	88.6 (55.5)	80.3 (49.6, 116)	
Vitamin D (µg/d)	3.4 (3.2)	2.5 (1.1, 4.6)	38.3 (24.4)
Fish fatty			
Food intake (g/d)	14.7 (16.9)	9.3 (2.4, 20.9)	
Vitamin D (µg/d)	2.1 (2.4)	1.3 (0.4, 3.1)	22.8 (20.9)
Fish lean			
Food intake (g/d)	36.6 (29.4)	29.7 (15.0, 50.5)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)	3.2 (3.6)
Fish remaining			
Food intake (g/d)	37.7 (29.2)	32.4 (18.3, 49.2)	
Vitamin D (µg/d)	1.1 (1.4)	0.7 (0.1, 1.5)	12.3 (13.2)
Butter			
Food intake (g/d)	26.1 (17.3)	23.4 (13.1, 35.3)	
Vitamin D (µg/d)	2.0 (1.2)	1.8 (1.1, 2.7)	31.5 (22.0)
Eggs			
Food intake (g/d)	15.8 (11.5)	15.3 (7.7, 19.4)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)	3.9 (5.0)
Dairy products			
Food intake (g/d)	343 (206)	321 (195, 458)	
Vitamin D (µg/d)	0.1 (0.1)	0.1(0.1, 0.2)	2.4 (7.1)

[1] Mean (SD)
[2] Median with 25th and 75th percentiles
[3] Mean % contribution (SD)

When dividing the population into users and non-users of cod liver oil, the pattern of contribution from the different food items changed (**Table 5**). For those that took cod liver oil, it was by far the main contributor of vitamin D. In the non-user group fish and fish products as well as butter/margarines were important sources of vitamin D. Eggs and dairy products also contributed more in the non-user group of cod liver oil.

Table 5. Sources and their mean contribution of vitamin D divided into users and non-users of cod liver oil

	User (n = 710)			Non-user (n = 1206)		
	Mean[1]	Median[2]	Contribution[3]	Mean	Median	Contribution
Vitamin D total	16.7 (8.9)	15.5 (10.1, 23.9)		6.0 (4.1)	5.2 (3.1, 7.8)	
Supplements total			55.7 (24.8)			4.4 (14.7)
Food intake (g/d)	5.0 (4.1)	5.1 (1.7, 6.5)		0.3 (1.4)	0.0 (0.0, 0.0)	
Vitamin D (µg/d)	10.6 (8.1)	11.0 (4.1, 15.1)		0.4 (1.6)	0.0 (0.0, 0.0)	
Cod liver oil			50.8 (25.7)			0
Food intake (g/d)	4.5 (3.5)	5.1 (1.4, 5.6)		0.0 (0.0)	0.0 (0.0, 0.0)	
Vitamin D (µg/d)	9.7 (7.5)	11.0 (3.0, 12.1)		0.0 (0.0)	0.0 (0.0, 0.0)	
Supplements rest			4.9 (12.3)			4.4 (14.7)
Food intake (g/d)	0.5 (1.9)	0.0 (0.0, 0.0)		0.3 (1.4)	0.0 (0.0, 0.0)	
Vitamin D (µg/d)	0.9 (2.6)	0.0 (0.0, 0.0)		0.4 (1.6)	0.0 (0.0, 0.0)	
Fish total			24.7 (18.3)			46.4 (24.0)
Food intake (g/d)	98.7 (58.3)	90.6 (59.2, 125)		83.2 (52.9)	74.9 (44.9, 111)	
Vitamin D (µg/d)	3.8 (3.3)	2.9 (1.4, 5.2)		3.1 (3.1)	2.3 (1.0, 4.2)	
Fatty fish			14.9 (14.3)			27.4 (22.7)
Food intake (g/d)	16.6 (16.9)	11.3 (3.5, 24.0)		13.6 (16.7)	8.2 (2.1, 19.4)	
Vitamin D (µg/d)	2.4 (2.4)	1.6 (0.5, 3.4)		1.9 (2.4)	1.2 (0.3, 2.8)	
Lean fish			1.8 (1.8)			4.1 (4.08)
Food intake (g/d)	40.3 (32.0)	34.1 (17.8, 53.8)		34.4 (27.5)	27.5 (15.0, 48.9)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)		0.2 (0.2)	0.2 (0.1, 0.3)	
Fish rest			8.0 (8.9)			14.9 (14.6)
Food intake (g/d)	41.9 (31.1)	36.5 (23.0, 52.9)		35.2 (27.7)	30.3 (16.0, 46.9)	
Vitamin D (µg/d)	1.2 (1.6)	0.8 (0.2, 1.7)		1.0 (1.4)	0.5 (0.1, 1.4)	
Butter/margarines			16.6 (13.2)			40.3 (21.4)
Food intake (g/d)	63.9 (37.8)	57.9 (36.0, 81.8)		55.9 (37.5)	48.1 (28.4, 75.2)	
Vitamin D (µg/d)	1.8 (1.2)	1.6 (0.8, 2.5)		1.7 (1.1)	1.5 (0.9, 2.4)	
Eggs			1.7 (1.7)			5.3 (5.7)
Food intake (g/d)	15.4 (10.8)	15.4 (7.7, 19.4)		16.0 (11.9)	15.3 (7.7, 19.4)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)		0.2 (0.2)	0.2 (0.1, 0.3)	
Dairy products			1.1 (1.1)			3.2 (3.5)
Food intake (g/d)	367 (208)	346 (217, 485)		328 (203)	301 (180, 435)	
Vitamin D (µg/d)	0.1 (0.1)	0.1 (0.1, 0.2)		0.1 (0.1)	0.1 (0.1, 0.1)	

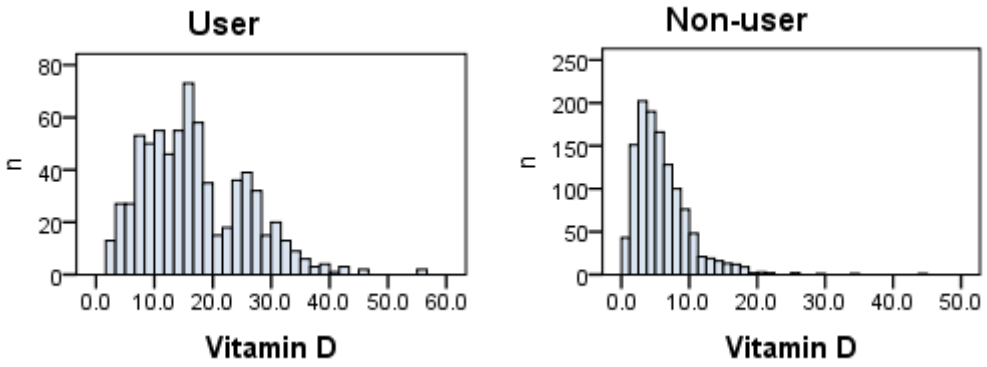
[1] Mean (SD) all such values

[2] Median (25th and 75th percentiles) all such values

[3] Mean % contribution (SD) all such values

Figure 4 shows the distribution of vitamin D intake when the population is divided in users and non-users of cod liver oil. More people had a higher intake of vitamin D in the user-group.

Figure 4. Distribution of vitamin D intake in users and non-users of cod liver oil



Cod liver oil was an important source of vitamin D in this population. **Table 6** shows that of those that took cod liver oil as a supplement, 76.1% reached the recommended intake of vitamin D, whereas only 12.4% of the non-users reached the recommended intake level. A significantly larger portion of the users reached the recommended intake levels of vitamin D compared to the non-users (X^2 test, P<0.001).

Table 6. Number of users and non-users of cod liver oil according to the Nordic recommendations of vitamin D intake

		Vitamin D intake			
		Total	**Low (<10 µg/d)**	**Adequate (≥10 µg/d)**	**%**
Cod liver oil	**User**	710	170	540	76.1
	Non-user	1206	1056	150	12.4
	Total	1916	1226	690	

Univariate ANOVA adjusted for sex, ApoE e4 variant allele, education, tHcy and total energy intake showed a significantly higher intake of total vitamin D in the users of cod liver oil compared to the non-users (**Table 7**).

Table 7. Vitamin D intake classified by the use of cod liver oil

	CLO						
	User			Non-user			
	n	**Mean**	**95% CI**	**n**	**Mean**	**95% CI**	***P*-value[1]**
Vitamin D intake	672	16.5	16.0, 16.9	1089	6.5	6.1, 6.8	<0.001

[1] ANOVA adjusted for sex ApoE e4 variant allele, education, tHcy and total energy intake

4.2 Cognitive performance

Upon defining a low cognitive test score as the tenth percentile (90th for the TMT-A) only 3 subjects were defined as scoring poorly on all of the cognitive tests. **Table 8** summarises the results from the cognitive testing. Z-scores are also included. The number of participants defined as scoring poorly on the different test varied. The number of people that scored poorly on at least one test was 678 comprising of 35.4% of the participants.

Table 8. Cognitive performance in the total population

	Total population (n = 1916)					
	Mean[1]	**Median[2]**	**Lowest**	**Highest**	**Cut-off[3]**	**%[4]**
S-task	15.3 (5.5)	15.0 (12.0, 19.0)	1	39	≤ 8 (184)	9.6
KOLT	35.4 (8.0)	35.0 (30.0, 41.0)	2	65	≤ 25 (180)	9.4
m-DST	10.4 (4.2)	9.0 (7.0, 13.0)	1	24	≤ 6 (154)	8.0
m-MMSE	11.6 (0.7)	12.0 (11.0, 12.0)	5	12	≤ 10 (155)	8.1
TMT-A	55.5 (32.5)	44.0 (36.0, 55.0)	16	248	≥ 109 (192)	10.0
m-BD	15.1 (2.2)	16.0 (16.0, 16.0)	1	16	≤ 12 (265)	13.8
Z-score	0.0 (1.0)	0.1 (-0.5, 0.7)	-5.0	2.7	≤ -1.3 (191)	10.0

[1] Mean (SD)

[2] Median (25th and 75th percentiles)

[3] Cut-off point for scoring poorly (number of subjects below that cut-off)

[4] Percent of the population defined as scoring poorly on the test

4.3 Adequate vs. low intake of vitamin D

In accordance with the Nordic recommendations, an intake of ≥10 µg/d was considered an adequate intake for this age group [18]. Sixty-four percent of the population did not meet the Nordic recommendations of vitamin D intake. More men than women were significantly classified as having an adequate intake of vitamin D (**Table 9**). The educational level as well as total energy intake was significantly higher in the adequate intake group compared to the low intake group. In an attempt to map out what could be the reason for the skewness in energy intake between the two vitamin D intake categories, we tested if the plasma variables for tHcy, vitamin B_{12}, folate, methylmalonic acid and creatinine were different between the adequate intake group and low intake group. tHcy was the only variable that differed between the two intake groups and was significantly higher in the low intake group (P = 0.027).

Four of the cognitive tests were significantly higher in the adequate intake group compared to the low intake group (S-task, m-DST, m-MMSE and Z-score). Plasma tHcy was significantly higher in the low intake group. There was no significant difference in ApoE *ε4* variant allele profile, smoking status, blood pressure, BMI, CVD or diabetes history when comparing the two intake groups. Plasma creatinine was borderline significantly higher in the adequate intake group.

Table 9. Adequate vs. low intake of vitamin D

	Adequate (≥10 µg)		Low (<10 µg)		
	n	**n (%) or mean (SD)**	***n***	**n (%) or mean (SD)**	***P* value[1]**
Sex (male)	690	393 (57.0)	1226	490 (40.0)	<0.001
Education ≤9 y	651	205 (31.5)	1128	460 (40.8)	<0.001
Daily smoker (yes)	690	91 (13.2)	1225	156 (12.7)	0.866
Number of cigarettes/d amongst smokers	91	9.5 (4.5)	156	10.6 (7.9)	0.638
BMI	690	25.9 (3.7)	1223	26.2 (4.0)	0.182
Total energy (kJ)	690	8671 (2272)	1226	6964 (2062)	<0.001
Vitamin D (µg/d)	690	18.8 (7.6)	1226	5.1 (2.4)	<0.001
Systolic blood pressure	690	146 (21)	1226	146 (20)	0.928
Diastolic blood pressure	690	78 (12)	1226	77 (12)	0.160
History of CVD (yes)	677	216 (31.9)	1192	411 (34.5)	0.279
Diabetes (yes)	678	39 (5.8)	1211	85 (7.5)	0.332
Depression score	664	3.3 (2.7)	1129	3.6 (2.8)	0.085
Cognitive test scores					
S-task	690	15.0 (5.3)	1226	15.8 (5.7)	0.001
KOLT	690	35.2 (8.2)	1226	35.8 (7.6)	0.097
m-DST	690	10.2 (4.2)	1226	10.8 (4.3)	0.002
m-MMSE	690	11.5 (0.8)	1226	11.6 (0.7)	0.047
TMT-A	690	57 (33)	1226	54 (32)	0.074
m-BD	690	15.1 (2.2)	1226	15.1 (2.1)	0.692
Z-score	690	0.96 (0.98)	1226	-0.05 (1.01)	0.002
Plasma variables and ApoE status					
tHcy (µmol/L)	690	11.7 (3.6)	1221	12.1 (3.9)	0.027
Creatinine (µmol/L)	690	78.3 (19.4)	1219	76.4 (18.6)	0.053
ApoE (allele present)	686	214 (31.2)	1216	392 (32.2)	0.645

[1] Pearson X^2-test corrected for continuity or Student's *t*-test

4.4 Unadjusted analyses including Student's *t*-tests and simple correlations

Men scored better on the TMT-A and women scored better on the KOLT (**Table 10**). None of the other cognitive tests differed according to sex. Intake of vitamin D was higher for men than for women.

ApoE *ε4* variant allele was associated with significantly lower test scores for KOLT, m-MMSE, m-DST and Z-score. The S-task, the KOLT and Z-score were significantly poorer for those with a history of CVD. The S-task, KOLT, m-DST and Z-score were significantly higher for the subjects without diabetes. Vitamin D did not differ significantly when testing for either ApoE *ε4* variant allele, history of CVD or diabetes (Table 10).

Table 10. Student's *t*-test for dichotomous variables in relation to cognitive test scores and vitamin D intake

	Sex		ApoE *ε4* variant allele		CVD		Diabetes	
	Mean difference[1]	*P* value[3]	Mean difference[2]	*P* value	Mean difference[2]	*P* value	Mean difference[2]	*P* value
COWAT	-0.04	0.862	-0.25	0.347	-0.57	0.035	-1.72	0.001
KOLT	-3.19	<0.001	-1.19	0.002	-1.67	<0.001	-1.66	0.024
m-DST	0.15	0.44	-0.52	0.012	-0.21	0.323	-0.91	0.021
m-MMSE	0.03	0.32	-0.1	0.011	-0.05	0.184	-0.1	0.132
TMT-A	-3.47	0.019	3.19	0.055	3.05	0.057	3.13	0.299
m-BD	0.14	0.16	-0.03	0.776	-0.12	0.261	-0.2	0.327
Z-score	-0.06	0.171	-0.13	0.007	-0.16	0.001	-0.29	0.002
Vitamin D	2.96	<0.001	0.25	0.529	-0.09	0.821	-0.53	0.493

[1] Men - women

[2] Sick - healthy

[3] *P* value from Student's *t*-test (all such values)

Table 11 shows Spearman's Rho correlation coefficients between continuous variables, the cognitive tests and vitamin D intake. Of the cognitive tests, vitamin D intake was correlated with S-task, m-DST, m-MMSE, TMT-A, and sum Z-score. Of the other variables vitamin D was associated with education, plasma tHcy, plasma creatinine, total energy intake and all of the food groups. At least four of the cognitive tests including sum Z-score were associated with the following variables: education, intake of total energy, depression score, supplements, fish total (including all fish and fish products), lean fish, fatty fish, dairy products, fruit, meat and meat products, cereals, vegetables, sweets and drinks (tea and wine). Coffee was not associated with vitamin D intake. Among the nutritional variables, fruit, meat and meat products, cereals, vegetables, sweets and drinks did not contain vitamin D and were considered potential confounders.

Table 11. Spearman's Rho correlation coefficients for continuous variables, the cognitive tests and vitamin D intake

	n	S-task	KOLT	m-DST	m-MMSE	TMT-A	m-BD	Z-score	Vitamin D
Vitamin D	1916	0.12**	0.03	0.08**	0.05*	-0.05*	0.04	0.10**	1.00
Education	1779	0.33**	0.11**	0.42**	0.20**	-0.27**	0.17**	0.40**	0.15**
tHcy	1911	-0.06**	-0.14**	-0.06*	-0.04	0.07**	-0.02	-0.11**	-0.05*
BMI	1913	-0.05*	-0.05*	-0.03	-0.02	-0.02	-0.02	-0.05*	-0.04
Depression score	1793	-0.06*	-0.10**	-0.10**	-0.01	0.10**	-0.04	-0.12**	-0.03
Smoking	1916	0.00	-0.01	-0.03	-0.02	0.07**	-0.07**	-0.05*	0.03
Creatinine	1909	0.03	-0.10**	0.01	0.03	-0.05*	0.05*	0.00	0.09*
Systolic blood pressure	1916	-0.05*	0.01	-0.03	-0.05*	0.01	0.01	-0.03	-0.01
Diastolic blood pressure	1916	-0.03	-0.02	-0.01	-0.00	-0.04	0.02	0.00	0.05*
Total energy	1916	0.06*	-0.03	0.06*	0.04	-0.01	0.05*	0.05*	0.48**
Supplements	1916	0.12**	0.05*	0.07**	0.04	-0.05*	0.04	0.10**	0.75**
Fish	1916	0.05*	0.05*	0.07**	0.07**	-0.07**	0.07**	0.09**	0.53**
Fatty	1916	0.06**	0.06**	0.06**	0.03	-0.06**	0.03	0.08**	0.50**
Lean and medium	1916	0.02	0.06**	0.04	0.08**	-0.05*	0.06*	0.07**	0.29**
Butter/oils	1916	0.02	-0.05	0.06**	0.04	-0.04	0.07**	0.05*	0.35**
Eggs	1916	-0.00	0.0.3	-0.05*	0.02	0.01	-0.02	-0.04	0.12**
Dairy products	1916	-0.05*	-0.02	-0.09**	-0.02	0.08**	0.02	-0.07**	0.14**
Fruit	1916	0.13**	0.12**	0.14**	0.08**	-0.09**	0.10**	0.18**	0.23**
Meat and meat products	1916	0.06**	0.01	0.07**	0.07**	-0.03	0.07**	0.07**	0.31**
Cereals	1916	0.07**	0.03	0.09**	0.05*	-0.10**	0.11**	0.11**	0.22**
Vegetables	1916	0.11**	0.09**	0.11**	0.11**	-0.09**	0.05*	0.15**	0.25**
Sweets	1916	0.09**	0.04	0.10**	0.02	-0.05*	0.07**	0.11**	0.15**
Drinks									
Tea	1916	0.10**	0.09**	0.13**	0.09**	-0.11**	0.05*	0.16**	0.06*
Wine	1916	0.23**	0.14**	0.23**	0.15**	-0.17**	0.09**	0.27**	0.16**
Coffee	1916	-0.06**	-0.03	-0.09**	-0.03	0.08**	-0.04	-0.10**	0.00

* Significant at 0.05 level

** Significant at 0.01 level

4.5 Linear regression analyses

Linear regression analyses adjusted for sex indicated that a significant association between quintiles of vitamin D intake as independent variable and the S-task, KOLT, m-DST, m-MMSE or the sum Z-scores as dependent variable existed (**Table 12**). After additional adjustment with ApoE ε4 variant allele, education, tHcy, and energy intake, the S-task and KOLT remained significantly associated with intake of vitamin D (Table 12). The association was markedly reduced compared to the sex-adjusted model. Further investigation revealed that inclusion of education and total energy intake accounted for the weakening of this association. In the final model, including adjustment for nutrients and disease variables, none of the cognitive tests remained significant.

Table 12. Linear regression analysis showing the relationship between vitamin D intake and the different cognitive tests

	B	SE	Partial *r*	*P*-value
S-task	0.452	0.535	0.114	<0.001
KOLT	0.433	0.129	0.077	0.001
m-DST	0.244	0.070	0.079	0.001
m-MMSE	0.028	0.012	0.052	0.022
TMT-A	-0.553	0.537	-0.02	0.304
m-BD	0.064	0.036	0.04	0.075
Z-scores	0.075	0.016	0.103	<0.001

Adjusted for sex

	B	SE	Partal *r*	P-value
S-task	0.227	0.099	0.055	0.021
KOLT	0.304	0.149	0.049	0.041
m-DST	0.007	0.076	0.00	0.930
m-MMSE	0.006	0.014	0.01	0.649
TMT-A	0.412	0.600	0.02	0.493
m-BD	-0.007	0.039	0.00	0.857
Z-scores	0.020	0.017	0.03	0.246

Adjusted for sex, ApoE *ε4* variant allele, education, tHcy and total energy intake

	B	SE	Partial *r*	*P*-value
S-task	0.176	0.098	0.043	0.074
KOLT	0.229	0.148	0.037	0.122
m-DST	-0.025	0.076	-0.008	0.740
m-MMSE	0.000	0.014	0.001	0.973
TMT-A	0.689	0.598	0.028	0.250
m-BD	-0.017	0.040	-0.010	0.676
Z-scores	0.008	0.017	0.011	0.637

Adjusted for sex, ApoE *ε4* variant allele, education, tHcy, total energy intake, cereals, meat and meat products, fruit, vegetables, sweets, tea and wine

4.6 Risk of poor cognitive test performance according to vitamin D intake

The risk of scoring poorly on a cognitive test according to quintiles of vitamin D intake was explored by the use of binomial logistic analysis. The upper quintile of vitamin D was used as the reference category.

In the model adjusted only for sex, when comparing the highest and lowest quintiles of vitamin D intake, there was an increase in risk for scoring poorly on the KOLT, m-DST, m-MMSE, and the sum Z-score (**Table 13**). In the second model, none of the *P trends* stay significant, but the increased risk of scoring poorly on the KOLT was significant at the lowest quintile of vitamin D intake. When introducing more covariates in the models, none of the tests remained significant (Table 13).

Table 13. Binary logistic regression analyses

		n	OR[1]	95% CI	OR[2]	95% CI	OR[3]	95% CI
S-task								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.84	0.51, 1.36	0.68	0.39, 1.16	0.67	0.39, 1.16
	5.96 - 9.19	384	0.73	0.44, 1.22	0.74	0.43, 1.28	0.73	0.42, 1.26
	3.58 - 5.95	384	1.08	0.67, 1.73	0.94	0.56, 1.59	0.89	0.52, 1.51
	≤ 3.57	382	1.40	0.88, 2.23	1.10	0.73, 2.29	1.12	0.66, 2.09
P trend			*0.095*		*0.318*		*0.540*	
KOLT								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.87	0.54, 1.46	0.89	0.52, 1.48	0.92	0.54, 1.57
	5.96 - 9.19	384	1.01	0.62, 1.67	1.00	0.59, 1.68	0.98	0.58, 1.66
	3.58 - 5.95	384	0.94	0.57, 1.57	0.71	0.41, 1.26	0.68	0.38, 1.21
	≤ 3.57	382	1.74	1.08, 2.80	1.81	1.04, 3.15	1.65	0.94, 2.89
P trend			*0.033*		*0.161*		*0.331*	
m-DST								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.86	0.46, 1.59	0.76	0.38, 1.50	0.75	0.38, 1.48
	5.96 - 9.19	384	1.21	0.68, 2.14	1.31	0.70, 2.45	1.28	068, 2.40
	3.58 - 5.95	384	1.78	1.04, 3.04	1.27	0.68, 2.37	1.21	0.65, 2.27
	≤ 3.57	382	1.90	1.11, 3.26	1.55	0.79, 3.05	1.43	0.72, 2.83
P trend			*0.001*		*0.092*		*0.156*	
m-MMSE								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.54	0.30, 1.00	0.39	0.19, 0.79	0.41	0.20, 0.83
	5.96 - 9.19	384	1.04	0.61, 1.75	0.95	0.54, 1.67	0.92	0.52, 1.63
	3.58 - 5.95	384	1.26	0.76, 2.10	0.94	0.54, 1.66	0.91	0.52, 1.61
	≤ 3.57	382	1.40	0.84, 2.32	0.88	0.47, 1.64	0.83	0.44, 1.55
P trend			*0.018*		*0.609*		*0.817*	
TMT-A								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.96	0.58, 1.57	0.79	0.46, 1.36	0.84	0.48, 1.45
	5.96 - 9.19	384	1.18	0.73, 1.89	1.20	0.73, 2.00	1.26	0.76, 2.11
	3.58 - 5.95	384	1.16	0.72, 1.86	0.91	0.53, 1.54	0.89	0.52, 1.51
	≤ 3.57	382	1.10	0.62, 1.66	0.78	0.43, 1.41	0.69	0.38, 1.26
P trend			*0.690*		*0.636*		*0.368*	
m-BD								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	0.99	0.65, 1.50	0.83	0.53, 1.31	0.84	0.53, 1.33
	5.96 - 9.19	384	0.83	0.54, 1.28	0.80	0.50, 1.26	0.80	0.51, 1.28
	3.58 - 5.95	384	1.02	0.67, 1.54	0.74	0.46, 1.17	0.72	0.45, 1.15
	≤ 3.57	382	1.30	0.87, 1.95	0.94	0.58, 1.53	0.86	0.53, 1.42
P trend			*0.215*		*0.605*		*0.404*	
Z-scores								
	≥ 15.63	382	ref		ref		ref	
	9.20 - 15.62	384	1.10	0.66, 1.85	0.96	0.55, 1.67	0.97	0.55, 1.71
	5.96 - 9.19	384	1.25	0.76, 2.08	1.19	0.69, 2.05	1.18	0.68, 2.05
	3.58 - 5.95	384	1.45	0.88, 2.37	0.94	0.53, 1.65	0.88	0.50, 1.55
	≤ 3.57	382	1.74	1.07, 2.83	1.31	0.72, 2.37	1.11	0.61, 2.02
P trend			*0.013*		*0.477*		*0.931*	

[1] Adjusted for sex

[2] Adjusted for sex, ApoE *ε4* variant allele, education, tHcy and total energy intake

[3] Adjusted for sex, ApoE *ε4* variant allele, education, tHcy, total energy intake, fruit, vegetables, meat and meat products, cereals, sweets, tea and wine

4.7 Intake of Cod liver oil, lean fish and fatty fish in relation to scoring poorly on an episodic memory test (KOLT)

Both fatty fish and cod liver oil were important sources of vitamin D (Table 4). There have previously been demonstrated a relationship between lean fish and KOLT score in this population [88]. Furthermore, the KOLT was the only test that was significantly associated with vitamin D intake in both linear and logistic regression analyses. The relationship between intakes of cod liver oil, lean fish, fatty fish and KOLT score were therefore further explored.

The mean intakes of vitamin D, lean fish, fatty fish and fish total, fish remaining, dairy products and butter/margarines were all significantly higher in the user group of cod liver oil (Student's *t*-test, all P-values < 0.001).

In multivariate linear regression analysis when adjusting for sex, both fatty fish intake and lean fish intake were significantly associated with KOLT score. Intake of cod liver oil was not significantly associated (**Table 14**). When further adjusting for ApoE *ε4* variant allele, education, tHcy and total energy, the association between intake of cod liver oil and KOLT score was weakened. The association between both fatty fish intake and lean fish intake in relation to KOLT score was only moderately reduced (Table 14). In the fully adjusted model, when further adjusting for other vitamin D containing food sources (butter/margarines, fish remaining, supplements remaining, eggs and dairy products) and keeping fatty fish and lean fish in the model, the association between cod liver oil and KOLT score was further weakened. The association between intakes of fatty fish and lean fish and KOLT score was still significantly associated and only slightly weakened (Table 14).

Table 14. Linear regression analyses exploring the relationship between intakes of cod liver oil, fatty fish, lean fish and KOLT score

	Modell 1[1]			
	B	**SE**	**partial**	**P value**
Cod liver oil	0.234	0.141	0.038	0.099
Fish fatty	0.527	0.127	0.094	<0.001
Fish lean	0.660	0.129	0.116	<0.001

	Modell 2[2]			
	B	**SE**	**partial**	**P value**
Cod liver oil	0.085	0.147	0.014	0.563
Fish fatty	0.498	0.135	0.087	<0.001
Fish lean	0.540	0.138	0.093	<0.001

	Modell 3[3]			
	B	**SE**	**partial**	**P value**
Cod liver oil	0.043	0.147	0.007	0.769
Fish fatty	0.375	0.141	0.064	0.008
Fish lean	0.436	0.142	0.073	0.002

[1] Adjusted for sex

[2] Adjusted for sex, ApoE e4 variant allele, education, tHcy and total energy intake

[3] Adjusted for sex, ApoE e4 variant allele, education, tHcy, total energy intake, butter/margarines, fish remaining, supplements remaining, eggs and dairy products

For the non-users of cod liver oil, the risk of scoring poorly on the KOLT increased when the intake of lean fish was low (0.1 – 25.0 g/d, P = 0.027) (**Table 15**). No significant relationship was found when the same analysis was performed with fatty fish as indicator variable.

Table 15. Logistic regression analyses exploring the relationship between intakes of lean fish and fatty fish, in users and non-users of cod liver oil, in regards to scoring poorly on the KOLT.

		User (*n* = 672)			Non-user (*n* = 1089)		
		n	OR	95% CI	*n*	OR	95% CI
KOLT							
Lean Fish[1]	≥ 50.1 g/d	198	*ref*		270	*ref*	
	25.1 - 50.0 g/d	242	0.76	0.36, 1.60	385	0.98	0.55, 1.74
	0.1 - 25.0 g/d	194	1.23	0.57, 2.63	345	1.92	1.08, 3.43
	0.0 g/d	38	0.71	0.15, 3.44	89	1.82	0.83, 3.99
P trend			*0.845*			*0.016*	
Fatty Fish[2]	≥ 20.1 g/d	204	*ref*		266	*ref*	
	10.1 - 20.0 g/d	165	0.74	0.77, 3.95	235	0.74	0.40, 1.38
	0.1 - 10.0 g/d	216	1.47	0.64, 3.38	368	0.90	0.52, 1.57
	0.0 g/d	87	1.87	0.69, 5.04	220	1.06	0.58, 1.69
P trend			*0.255*			*0.743*	

[1] Adjusted for sex, ApoE *ε4* variant allele , education, tHcy, total energy and fatty fish

[2] Adjusted for sex, ApoE *ε4* variant allele, education, tHcy, total energy and lean fish

When further adjusting for other sources of vitamin D (butter/margarines, supplements remaining, fish remaining, eggs, and dairy products), the model weakened, but the same intake category for lean fish (0.1 – 25.0 g/d) remained significant (**Table 15**) in non-users of cod liver oil.

Table 16. Logistic regression analyses exploring the relationship between intake of lean fish and fatty fish in users and non-users of cod liver oil in regards to scoring poorly on the KOLT. Multiple adjustments

		User (*n* = 672)			Non-user (*n* = 1089)		
		n	OR	95% CI	*n*	OR	95% CI
KOLT							
Lean Fish[1]	≥ 50.1 g/d	198	*ref*		270	*ref*	
	25.1 - 50.0 g/d	242	0.74	0.35, 1.57	385	0.96	0.53, 1.71
	0.1 - 25.0 g/d	194	1.17	0.54, 2.54	345	1.81	1.00, 3.26
	0.0 g/d	38	0.69	0.14, 3.44	89	1.72	0.78, 3.80
P trend			*0.933*			*0.031*	
Fatty Fish[2]	≥ 20.1 g/d	204	*ref*		266	*ref*	
	10.1 - 20.0 g/d	165	1.95	0.84, 4.51	235	0.71	0.39, 1.34
	0.1 - 10.0 g/d	216	1.52	0.65, 3.58	368	0.85	0.48, 1.49
	0.0 g/d	87	1.81	0.65, 5.03	220	1.00	0.54, 1.84
P trend			*0.296*			*0.886*	

[1] Adjusted for sex, ApoE *ε4* variant allele, education, tHcy, total energy, fatty fish, butter/margarines, fish remaining, supplements remaining, eggs and dairy products.

[2] Adjusted for sex, ApoE *ε4* variant allele, education, tHcy, total energy, lean fish, butter/margarines, fish remaining, supplements remaining, eggs and dairy products.

When not using users/non-users of cod liver oil as a selection variable, but instead including intake of cod liver oil as an adjustment variable, and still using lean fish as an indicator variable, the increased risk of scoring poorly on the KOLT, when adjusting for sex, ApoE *ε4* variant allele, education, tHcy, total energy, fatty fish and other sources of vitamin D, was still almost significant for reduced lean fish intake (0.1 – 25.0 g/d, OR = 1.59, 95% CI: 0.98, 2.47, P = 0.059).

5. Discussion

5.1 Methodological considerations

The validity of a study is often discussed in terms of internal and external validity. Internal validity implies the degree to which the estimated effect or association between exposure and outcome is true or valid for the source of the study [104]. In evaluating internal validity one needs to consider the likelihood that alternative explanations such as bias or confounding could account for the findings. External validity refers to generalisation of the study results [104].

5.1.1 Study design

Observational studies are used to study factors or exposures that cannot be controlled by the investigator [105]. There are different types of observational studies, and the cross-sectional design is one of them. In a cross-sectional study, all the information is collected at the same time. The particular difficulty associated with cross-sectional studies when looking at associations with disease concerns the sequence in time of the disorder of interest and the possible risk factor. Because the data is collected at the same time it is not possible to draw a clear inference of causality [105].

It is complicated to perform randomised controlled studies on cognitive decline. When a person start to show signs of cognitive impairment or dementia, intervention is already too late as the subject might have already changed his/her habits as a result of the disease. It becomes a near impossible task to conclude whether the person’s habits are a result of the disease or if the disease has developed secondary to the individual’s habits. Because dementia is a progressive disease, the cross-sectional design of the present study serves as a substantial limitation.

5.1.2 Statistical aspects

An association between an exposure and outcome, or lack of association might be the result of chance. Sample size is directly related to chance. The probability that the results are due to chance decreases as the sample size increases [104]. Our study is one of the larger cohorts on cognition among elderly. Furthermore, because of a large sample size, very small differences were detected as significant. Whether a small effect size is considered important depends on the context of measurements compared. In medical and nutritional research, small effect sizes usually reflected by small increases of risk are often considered clinically relevant [104]. The large sample size is considered a strength in the present study.

5.1.3 Bias and confounding

Recruitment bias

Recruitment bias denotes errors that result from systematic differences in characteristics between those who participated in the study and those who did not [104].

Apart from affecting the observed prevalence of a disorder, the choice of sample may have a strong effect on the observed relation with other factors. The validity of the extrapolation depends crucially on the representativeness of the sample. It is an innate weakness of most observational studies that the sample is not representative of the population [105].

Non-participation can pose as a problem in cross-sectional studies. Many studies have found that there are marked differences (demographic and health related) between those who do or do not respond to a questionnaire, with the non-responders usually being less healthy [105]. Socio-demographic analyses of drop-outs and attendees in the HUSK study at large have been performed in regards to income, education, employment and disability and social pensions; (http://www.uib.no/isf/husk/Vedlegg_dokumenter/FrafallsanalyseHUSK9799.pdf). It showed that non-participants had significantly more unfavourable lifestyle characteristics. An under-representation of individuals with adverse risk factors, such as lower education, may leave the results non-representative.

In the present study, because 71% of the study participants volunteered for cognitive testing, recruitment bias may have been an issue. Differences between those that attended and those that did not attend the cognitive sub-study have been reported elsewhere [91]. A significantly higher percentage of the non-participants showed presence of ApoE *ε4* variant allele, less education, higher levels of tHcy and lower vitamin B_{12} in serum. Furthermore, a higher percentage of the non-participants had CVD/hypertension [91]. More information on the study population can be found on the internet: (www.uib.no/isf/husk/Vedlegg_dokumenter/Cognitive_Sub_study.pdf)

Confounding

Confounding implies that the estimated effect of the exposure is mixed together with the effect of another factor, and so distorts the observed exposure-outcome association [106]. Confounding, or conclusion/distortion of effects, is of concern in all observational studies, but in contrast to selection and recall bias, confounding can be adjusted for in the analyses. The management of possible confounding relies on proper measurements and analytical approaches as well as knowledge of biological mechanisms [105]. In principle, a confounder should be associated with both the exposure and the outcome to exert a confounding effect and a factor that represents a step in the causal pathway between exposure and outcome should not be treated as a confounder [105]. ApoE *ε4* variant allele and education are considered strong potential confounders of cognitive decline with age [107, 108]. Furthermore, foods are not consumed individually, but as part of a diet; therefore, confounding by other food items is always an issue in studies utilising dietary assessments. In the statistical analyses, we included adjustments for several potential confounders, but residual confounding cannot be excluded.

Sun light exposure

Sun light exposure could possibly have a confounding effect on cognitive test score. It was however chosen to not adjust for this variable in the final analyses. UVB wavelengths that are optimal for vitamin D production in the skin differ according to altitude, latitude and weather conditions [109, 110]. Norwegian people commonly travel to the mountains during the winter months and typically during Easter holiday [111]. UVB radiation has been shown

to be stronger at higher altitudes leading to better conversion of pre-vitamin D in the skin [110]. Furthermore, we did not have information on the use of tanning beds, which have been shown to be highly effective when it comes to the endogenous production of vitamin D [112, 113]. Also, people in Norway typically exhibit sun-seeking behaviour as they travel a lot to sunnier parts of the world, and especially during the winter months [111]. In addition, people in the HUSK study come from the western part of Norway, and the weather in this part of the country tend to be cloudy and rainy even during the months of summer. One study found that the conversion of vitamin D was reduced with as much as 20% on a cloudy day compared to a sunny day in the same month [110]. In addition, people's capacity to make vitamin D in the skin is individually different, and also often reduced in the elderly [114]. Although information of month of cognitive testing was available, the abovementioned uncertainties related to sun-light exposure, led to the decision of omitting this variable from the final analyses. Also, adjusting for this variable did not change the results.

Energy intake

According to the Nordic Recommendations the energy intake in this age group should be 10600 kJ (PAL = 1.6) for men and 8500 kJ for women (PAL = 1.6) [18]. These reference values are used on the basis that these adults are generally healthy and not institutionalised. The population in the present study had an energy intake of approximately 2000 kJ fewer than what is recommended. This was a consistent finding in both genders.

The total energy intake was significantly higher in the adequate intake group of vitamin D compared to the low intake group. In theory, if the energy intake is lower in the low-intake group of vitamin D, this would become apparent in the serum values of the different vitamin markers, as the intake of those vitamins would probably be lower as a result of lower energy intake. When testing for differences in serum values between the two vitamin D intake categories, only tHcy differed significantly, and were higher in the low intake group. One explanation for the skewness in energy intake might be that the low-intake group had a significantly larger proportion of women than men, and the women in this population do indeed have a significantly lower energy intake than the men (as would be expected). We

have no explanation for the apparent low intake of energy in this population, but total energy intake and gender were adjusted for in the analyses.

Information bias

Information bias arise when the information collected from the study participants regarding exposure or outcome is incorrect and thus leads to systematic error in the effect estimation [104]. Studies requiring recall of detailed dietary habits are prone to this problem, often referred to as recall bias [105].

The FFQ used in the present thesis has been validated by several studies [81, 82, 115]. Validation studies include 14 day weighed records with the intakes calculated from the FFQ in a group of 38 elderly women [115], the correlation between self-reported dietary intake of fish and essential omega-3 fatty acids in plasma phospholipids among 579 men and women [81], and 14-day weighed records with the intakes calculated from the FFQ in a group of 125 men [82]. These studies show that the questionnaire is suitable to be used as an assessment tool when it comes to the estimation of intake of a wide range of micronutrients. None of the previously mentioned validation studies have, however, used vitamin D as a biomarker.

Dietary assessment is a field of research that has several pitfalls associated with it. Participants might forget what they eat, or report what they think is expected of them. An FFQ can merely give the information on how the individual perceives his/her diet. It can never be an objective type of measurement. FFQs do, however, allow for a large population sample as they are less time consuming and expensive than other methods for mapping out peoples dietary habits, such as 24 hour recall or the weighing of food.

People suffering from dementia or other forms of cognitive impairments might have changed their diet as a result of the disease. Consequently, self-reported dietary data collected from people that are cognitively impaired or demented may be less reliable. However, because these were free-living subjects and the vast majority were not impaired, it seems unlikely that this would have a major impact on the findings.

Data on serum vitamin D levels were not available in the present population, and serves as a limitation in the study. However, methods for measuring vitamin D in serum are under scrutiny as they show large discrepancies between method variation [1]. An evaluation of seven methods using 291 EDTA plasma samples showed that all methods except HPLC demonstrated significant negative bias compared with the “gold standard” liquid chromatography-mass spectrometry [116]. Serum levels are an objective measure and it would have been of great value to have information on both dietary intake and serum levels.

The cognitive tests used in this thesis have been well validated [95, 117-120]. These tests, although frequently used in the clinic, are however never the sole grounds for diagnosing someone with dementia [121]. Psychiatric evaluation as well as input from the close family of the individual are emphasised to a high degree. For research purposes though, the tests as screening instruments serve as valuable tools for the investigator. The size of the test battery in this study is of particular importance as it made it possible to investigate if some areas of cognition were more affected than others.

5.1.4 Generalisation

Generalisation, or external validity, refers to whether a study can produce inferences regarding a target population beyond the population sample of the study [104]. Because comparisons between those who were cognitively tested and those who were not revealed differences between the groups, it is unlikely that the study population is fully representative of the general elderly population. One should therefore be careful not to extrapolate the results. However, the strength of this study is the large sample size, its recruitment from the general population and the comprehensive cognitive test battery. Thus, even if the cognitive study population was modestly healthier and differed in certain characteristics from those that did not attend, we still believe that the subjects represent a relatively large section of the general elderly population in Western Norway.

5.2 Discussion of specific results

In a large population-based study of elderly people, we found that even though the intake of vitamin D rich food items such as fatty fish and cod liver oil were high, the total intake of vitamin D in the study population were in general low, and a high portion of the participants did not meet the Nordic recommendations. Furthermore, for those that took supplemental cod liver oil, the intake was significantly higher than for those who did not. We found a significant association between vitamin D intake and cognitive test scores for several of the cognitive tests in the test battery (S-task, KOLT, m-DST and Z-score). Moreover, the risk of scoring poorly on several cognitive tests increased when the vitamin D intake was low. Adjustment for relevant covariates did, however, markedly reduce the strength of the association. Also, the results show that cod liver oil intake was not associated with KOLT score, but that lean fish and fatty fish both were associated. In addition, we found that for non-users of cod liver oil, the risk of scoring poorly on the KOLT was associated with low intake of lean fish, while fatty fish, a rich source of vitamin D, did not contribute.

5.2.1 Intake of vitamin D in the elderly

The contributing sources of vitamin D were found to be fish and fish products (especially fatty fish), cod liver oil and fortified butter/margarines. Our population consumed high amounts of vitamin D-containing foods such as cod liver oil and fish and fish products compared to other studies [122-124].

The vitamin D intake in the present population showed a wide range (0.5 to 56.1µg/d). When referring to the Nordic Recommendations, 64.0% were defined as having a low intake of vitamin D. According to the American Recommendations for this age group, which is ≥15.0 µg/d [125] 77.6% would be defined as having a low intake with only 22.4% having an adequate intake.

Intake of vitamin D amongst the elderly populations is lower than the recommended intake level in all the Nordic countries [126]. In theory, it is possible to design a diet that would meet the recommendations of ≥10 µg/d, but the fact remains that it is difficult to achieve these amounts without supplementation [15]. Data from NHANES 1999-2000 showed that

total vitamin D intake from food sources across all age groups ranged from 3.8 – 6.9 µg/d, and that few older adults did achieve recommended vitamin D intakes [127]. It has been proposed by different researchers that elderly with little or no sun light exposure should receive a supplement of 10 µg/d in addition to their dietary intake [15, 128, 129].

Fortification and supplement use

In the present population, the users of cod liver oil had a significantly higher intake of vitamin D than those that did not take cod liver oil as a supplement. A high percentage (76.1%) of those that took cod liver oil as a supplement, did in fact reach the recommended intake level of vitamin D. In contrast, only 12.4% of the non-users of cod liver oil reached the recommended intake level of vitamin D.

O'Donnel et al found in their meta-analysis reviewing 11 randomised controlled trials that vitamin D fortified foods improved vitamin D status in adults in the United States [130]. Furthermore, Calvo et al reported that fortified foods provided 65 – 86% of the total daily vitamin D intake from foods [20]. Moore et al found, however, that even though USA fortify several foods such as orange juice, milk and yoghurt, margarine, flours and ready-to-eat breakfast cereals, the intake is still much lower than the recommended daily allowance (RDA) [125].

As mentioned in the introduction, there are several challenges for the elderly part of the population in regards to reach a satisfactory vitamin D status. Age-related biological changes such as a reduced capacity to synthesise vitamin D in the skin as well as a lower conversion of the hormone in the kidneys, combined with the fact that this population reside in Norway at high latitude where endogenous synthesis is very low many months of the year, increase the necessity for an adequate intake. Furthermore, many elders are institutionalised and receive little or no sunlight exposure.

Even though this population had a high intake of vitamin D-containing foods and supplements, the majority were defined as having a less than adequate intake. We found that for those not taking cod liver oil, fortified foods (butter and margarine) was an important source of vitamin D. Furthermore, we found that supplementation in the form of cod liver

oil was successful in regards to reaching the recommendations. Our data suggest that supplementation combined with fortification would probably be required in order to reachthe recommended intake levels of vitamin D.

5.2.2 Intake of vitamin D and cognitive test performance

We found that a low intake of vitamin D increased the risk of scoring poorly on several of the cognitive tests (KOLT, m-DST, m-MMSE and sum Z-scores). After multiple adjustments, the KOLT (episodic memory) and S-task (verbal fluency) remained significant for linear regression analysis, whereas only the KOLT was significantly associated with one of the quintile intakes of vitamin D in logistic regression analysis.

An extensive body of evidence supports a role for vitamin D beyond the classical function in calcium homeostasis. Epidemiologic observational studies have revealed a beneficial role for vitamin D in muscle function, cardiovascular health, diabetes, and cancer prevention [1]. More recently, evidence is emerging regarding a potential beneficial role of vitamin D in cognitive function [31].

Deficiency studies in animal models and epidemiologic investigations have supported a role for vitamin D in neurodegenerative disorders such as dementia.

Biological evidence

As mentioned in the introduction, vitamin D exhibits functional traits that may prove neuroprotective through antioxidative mechanisms, neuronal calcium regulation, immuno-modulation, enhanced nerve conduction and detoxification mechanisms [54, 56, 70]. The vitamin D receptor and catalytic enzymes are co-localized in the areas of the brain involved in complex planning, processing, and the formation of new memories [45, 50, 64]. These findings potentially link vitamin D to neurocognitive function.

Whereas some studies have reported no observed impairments in working memory or anxiety in the VDR-Knock Out (VDR-KO) model [50], others have been able to show such discrepancies in the VDR-KO phenotype. Symptoms such as anxiety-like behaviour and behavioural impairment were observed by Kalueff et al [52, 53]. In embryonic animal

models it has also been discovered that vitamin D deficiency may result in morphological brain changes and memory and learning deficits [49, 131].

Clinical evidence

While *in vitro* and animal models suggest neuroprotective benefits from vitamin D upon exposure, there are inconsistencies in the clinical literature related to vitamin D and cognitive function in the elderly.

One case-control study with a substantial cognitive test battery found that there were no significant positive association between 25(OH)D concentration and cognitive performance. They did however report that a low level of serum 25(OH)D was significantly associated with a high depression score [41]. Two other cross-sectional studies did discover significant positive associations between serum 25(OH)D and cognitive performance [38, 39]. Another study, also with a cross-sectional design, found no significant positive association between 25(OH)D concentration and cognitive abilities determined from different cognitive tests [42]. Oudshoorn et al performed a cross-sectional study and stated that there was a significant positive association between 25(OH)D and scores on the Mini Mental State Examination [37]. LLewellin et al established in their cross-sectional study by using data from the Health Survey for England 2000 (HSE) that low serum 25-hydroxyvitamin D is associated with increased odds of cognitive impairment [132]. Slinin et al found little evidence of independent associations between lower 25(OH)D levels and baseline global and executive cognitive function or incident cognitive decline in their cohort study of community dwelling elderly men [133].

Buell et al states that to test cognitive function in relation to vitamin D a comprehensive cognitive test battery and a large sample size is necessary [31]. They found, using data from the NAME study [134], a large cross-sectional study with 1200 participants and an extensive test battery, that 25(OH)D was associated with both global and specific aspects of cognitive function [135].

McCann et al found in their review that even though mechanistic and biological evidence strongly suggests that Vitamin D is involved in brain development and critical brain

functions, it was difficult to demonstrate obvious effects of vitamin D deficiency on cognitive endpoints [136]. They do however conclude from the overall evidence that supplementation to ensure adequacy is needed in vulnerable populations such as the elderly [136].

Annweiler et al performed a meta-analysis reviewing 127 articles where they aimed to describe the relationship between vitamin D and the nervous system throughout the different stages of life. They state that of the studies reviewed, there are arguments in favour of a life long role of vitamin D on the nervous system. They go on to say that in older adults, hypovitaminosis D has been associated with neuromuscular disorders, dementia and Parkinson's disease. They conclude that vitamin D has been associated with many neurological functions and its deficiency with dysfunction. Low serum 25-hydroxyvitamin D concentrations can potentially be reversed. This simple and low-cost correction might contribute to the prevention of various neuropsychiatric disorders [137].

5.2.3 Intakes of cod liver oil, lean fish and fatty fish in relation to cognitive performance

In theory, if vitamin D is protective of cognitive decline, vitamin D containing foods would also have a protective effect on cognition. We found that the food items that contribute substantially to the total intake of vitamin D were cod liver oil, fatty fish, and butter and margarines. Incidentally, the intake of lean fish is very high in the present population. In this cohort, lean fish, which is not a good source of vitamin D appeared to be more important for cognitive performance than fatty fish and cod liver oil, both of which are substantial providers of vitamin D.

As mentioned earlier, it has previously been shown in this cohort that effects of fatty fish and lean fish on cognition were comparable, but that when restricting the significance level to $P<0.001$ in a multiple adjusted model, only the association between lean fish and the KOLT remained ($P<0.001$) [88]. Data from that same study showed that subjects whose mean daily intake of fish and fish products was ≥10 g/d had significantly better mean test scores and a lower prevalence of poor cognitive performance than did those whose intake

was <10 g/d. Furthermore, they found that the effect was more pronounced for non-processed lean fish and fatty fish. They concluded from their study that in the elderly, a diet high in fish and fish products is associated with better cognitive performance in a dose-dependent manner [88].

The population in HUSK have an intake of lean fish that is high compared to other studies [124, 138]. A diet rich in fish might be part of other lifestyle choices and a dietary pattern that is protective of cognitive decline [139, 140]. Data from HUBRO suggest that people with higher/more education are more likely to take supplements [129]. In the present population, the intake of fish and fish products and supplements were higher for the users of cod liver oil.

Studies have come up with conflicting results when it comes to the protective effects of fish and fish oils in regards to cognitive impairment. Dangour et al were not able to show any protective effect of fish oil supplements in their randomised controlled trial. The trial only ran for 24 months and so it was speculated that the intervention period was too short to show any effect [141]. Devore et al found, using data from the Rotterdam study that a moderate consumption of fish and omega-3 poly-unsaturated fatty acids (PUFAs) were not associated with long term risk of dementia, and that there were little or no difference if the subjects consumed fatty fish, lean fish or omega-3 PUFAs [142].

A diet high in fish and fish products may replace other unhealthy nutrients such as saturated fatty acids from meat. Indeed, studies have found that a dietary pattern that resembles the Mediterranean diet, which is high in fish, vegetables, fruits and nuts, olive oil (mono unsaturated fatty acids), cereals, low in meat and dairy products, and moderate consumption of alcohol, might be protective of cognitive decline [143].

Food pattern analysis

Dietary pattern analysis is a method that makes it possible to examine the relationship between diet and the risk of chronic diseases. Rather than looking at the effects of individual nutrients or foods, dietary pattern analysis examines the diet on a whole by

applying statistical methods such as factor analysis, cluster analysis and dietary indices [144].

Dietary patterns represent a broader picture of food and nutrient consumption, and may for that reason be more predictive of disease risk than individual foods or nutrients. The present study has analysed the intake of vitamin D as a single nutrient in relation to cognitive function. There are several limitations in regards to single nutrients or single foods in relation to disease. Firstly, people do not eat isolated nutrients. Single nutrients are part of food items, food items are ingested as meals, and both foods and meals are complex combinations of nutrients that are likely to be interactive or synergistic [145]. Secondly, the effect of a single nutrient may be too small to detect, but the cumulative effects of multiple nutrients included in a food pattern might be adequately large to be noticeable [146]. Finally, as nutrient intakes are commonly associated with certain dietary patterns [147, 148], single nutrient analysis may be confounded by the effect of dietary patterns [144]. Adjustment for nutritional covariates in multivariate analyses may leave residual confounding effects because the dietary components may interact with each other. Dietary pattern analysis may serve as a complimentary approach to single nutrient analysis and can be used as a covariate when examining a specific nutrient to determine whether the effect of the nutrient is independent of the overall dietary pattern [144].

Observational epidemiological studies are recognising dietary pattern as potentially being protective of cognitive decline [143, 149].

Gu et al examined the effects of dietary pattern in relation to the development of Alzheimer's disease in a cohort consisting of over 2000 community-based elderly New Yorkers. They found a strong relationship with a specific dietary pattern and reduced risk of developing Alzheimer's disease. The diet was characterised by higher intakes of salad dressing, nuts, fish, tomatoes, poultry, cruciferous vegetables, fruits, and dark and green leafy vegetables and a lower intake of high-fat dairy products, red meat, organ meat, and butter. They concluded that simultaneous consideration of previous knowledge regarding potentially Alzheimer's-related nutrients and multiple food groups can aid in identifying food combinations that are associated with Alzheimer's risk [139].

6. Conclusions and implications

In a population-based study with a high intake of vitamin D containing foods, we found that the sources that contributed mostly to the total intake of vitamin D were fish and fish products, supplements in the form of cod liver oil, and butter and margarines. Furthermore, the intake of vitamin D was significantly higher for those that took cod liver oil as a supplement. Weak associations between vitamin D intake from foods and supplements, and cognitive function were found in both multiple linear and logistic regression analyses. Another finding was that for non-users of cod liver oil, a low intake of lean fish was associated with having an increased risk of scoring poorly on the KOLT (episodic memory), whereas intake of fatty fish or cod liver oil (both of which are rich sources of vitamin D) was not significantly associated. From this research project, it remains unclear whether it is vitamin D in itself, food items or dietary pattern that is protective when it comes to cognitive decline.

The strengths of the present study were a large sample size as well as a comprehensive cognitive test battery. The cross-sectional design together with the lack of 25(OH)D serum values serve as substantial limitations.

Whereas clinical studies show conflicting results, biological evidence supports a role for vitamin D in the protection of cognitive decline. Because dementia is a disease that develops over time, it seems likely that prevention in the form of diet would have to be life long. The pressing need to find preventative measures for this detrimental disease warrants large, long-term, population-based prospective studies as well as randomized controlled trials using both intake data as well as 25(OH)D in serum. Also, perhaps it would be wise to utilise dietary pattern analysis in addition to single nutrient analysis.

Finally, the topic of vitamin D and cognition is relatively new and future studies should aim at providing greater understanding of the biological effects of vitamin D on cognitive impairment.

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Article

The following article is in preparation, and is in the process of being read through by co-authors.

Cognitive performance among the elderly and intake of vitamin D:

The Hordaland Health Study

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Short running head: “Vitamin D intake and Cognition in the elderly”

ABSTRACT

Background: Increasing evidence suggests that vitamin D may be protective in the development of cognitive impairment and dementia in older subjects.

Objective: To examine the cross-sectional relationship between dietary intake of vitamin D and cognitive performance.

Design: Subjects (n =1916) aged 70-74 years, were recruited from the general population in Western Norway and underwent cognitive testing. The cognitive test battery included the Kendrick Object Learning Test (KOLT), Trail Making Test (part A), modified versions of the Digit Symbol Test, Block Design, Mini-Mental State Examination, and Controlled Oral Word Association Test (COWAT). Intake of vitamin D was calculated from a food frequency questionnaire.

Results: Sixty-four percent of the population did not meet the Nordic recommendations of vitamin D intake (≥ 10 μg/d). In adjusted linear regression analyses, only COWAT and KOLT were significantly, but weakly associated with intake of vitamin D. Logistic regression analyses showed that the risk of scoring poorly on the KOLT was significantly increased when the intake of vitamin D was low. Further investigation suggested that a low intake of lean fish in subjects that did not consume cod liver oil was associated with increased risk of scoring poorly on the KOLT.

Conclusions: In the elderly, a low vitamin D intake was associated with increased risk of scoring poorly on episodic memory and verbal fluency. In non-users of cod liver oil, episodic memory was negatively affected by a low intake of lean fish. Fish as a food item and dietary pattern may be more protective when it comes to cognitive decline than vitamin D as a single nutrient.

KEY WORDS Cognitive deficit, cognition, elderly, vitamin D, cholecalciferol

INTRODUCTION

Vitamin D deficiency causes rickets and ostemalacia [1]. In recent years, observational studies have shown that an optimal vitamin D status may also be associated with reduced risk of autoimmune diseases, diabetes type 2, cancer, cardiovascular disease (CVD) and cognitive impairment [2-6].

Vitamin D is a pro-hormone that is produced in the skin through a photolytic process induced by sunlight exposure (UVB 290-320 nm) [7]. There are two forms of vitamin D; cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2). Vitamin D3 is produced in the skin and it also occurs naturally in a small range of foods, whereas vitamin D2 derives from plants and yeast. Through two enzymatically regulated hydroxylation reactions active vitamin D (1,25-dihydroxyvitamin D, calcitriol) is produced in the liver and kidney, respectively [8].

Elderly are at particular risk for developing vitamin D deficiency due to reduced capacity to synthesise vitamin D in the skin [9]. Also, many elderly are institutionalised and therefore less exposed to sunlight [10]. It has been estimated that 40-90% of the elderly worldwide have vitamin D insufficiency (<75 nmol/L) [11]. In addition, people living in high latitudes often have a reduced endogenous production of vitamin D as the UV wavelengths are less than optimal for dermal production of the vitamin [12]. These findings suggest that an increase in vitamin D intake may be necessary in this section of the population.

Vitamin D in the diet is almost solely found in fatty fish and fish oils [7]. Supplementation and fortification are important contributors to the total intake of vitamin D [13].

Studies have confirmed that an increase in vitamin D intake leads to an increase of vitamin D in serum [14-16]. This present study focuses on the intake of vitamin D in relation to cognition in older subjects using data from the Hordaland Health Study (HUSK), a population with high intake of fish and fish oils.

SUBJECTS AND METHODS

Study population

The HUSK study was conducted from 1997 to 1999 as a collaboration between the University of Bergen, University of Oslo, local health services, and the Norwegian Institute of Public Health. In a subsample of the study, 4338 individuals born in 1925–1927 who had participated in the Hordaland Homocysteine Study in 1992–1993 [17], were re-invited to participate in HUSK. Recruitment into the Cognitive Sub-study is described on the Web (Internet: www.uib.no/isf/husk/Vedlegg_dokumenter/Cognitive_Sub_study.pdf). A total of 2155 subjects completed the cognitive test battery. Of those, 1991 individuals completed a food-frequency questionnaire (FFQ). Participants with a very low energy intake (< 3000 kJ for women; < 3300 kJ for men), or very high energy intake (≥ 15000 kJ for women; ≥ 17500 for men) were excluded from the analyses [18], leaving a total of 1916 subjects that were included in the present study. All participating subjects gave their written informed consent. The study protocol was approved by the Regional Committee for Medical Research Ethics of Western Norway.

Data collection

Cognitive testing was performed at the study location by trained nurses after the standard cardiovascular examinations of the National Health Screening Service were completed [17]. The cognitive test battery included 6 tests. The abridged version of the Controlled Oral Word Association Test (COWAT, called also S-task), a test of verbal fluency and psychomotor speed [19]; the Kendrick Object Learning Test (KOLT), a test of episodic memory [20]; the modified version of the Digit Symbol Test (m-DST) which was designed to measure focused attention, visuomotor coordination, and psychomotor speed [21]; the Trail Making Test part A (TMT-A), a test of visual conceptual and visuomotor tracking [22]; the modified version of the Block Design

test (m-BD), a test of visuospatial and motor skills [21]; and lastly, the modified version of the Mini-Mental State Examination (m-MMSE) which is a test of global cognition [23]. Z-scores were calculated for all of the tests except for the m-MMSE, and combined together into one variable. This sum Z-score variable represents global cognition, but in contrast to m-MMSE it has the advantage of being normally distributed, and without ceiling effect.

Dietary habits

To assess habitual food composition, a modified version of a comprehensive FFQ created at the Department of Nutrition, University of Oslo [24], was handed out on the day of the examination and filled out later at home by the participants and then mailed to the HUSK project Centre in Bergen. The FFQ was designed to give information about food intake during the past year. The questionnaire included 169 food items that were grouped according to Norwegian meal patterns. The frequency of consumption was given per day, week, or month. The portion sizes were given as household measures or units such as slices or pieces. In addition to food groups the questionnaire also included questions about dietary supplement intake, in which the product names of the most used supplements in Norway were considered. The use of cod liver oil was reported as seasonal use (during the whole year or only winter half of the year), frequency per week, and amount per time. The subjects were advised to estimate an “average” of amounts of food. The intake per person according to food group and nutrients was calculated by the use of a food database and software system developed at the Department of Nutrition, University of Oslo (Kostberegningssystem, KBS, version 3.2; University of Oslo, Oslo, Norway) [24]. The FFQ has been validated in several studies [24, 25].

Covariates

At baseline, participants underwent the standard cardiovascular examinations of the National Health Service. Several self-administered questionnaires focusing on cardiovascular risk factors, lifestyle factors, and dietary habits were used. A history of CVD was defined as self-reported information at baseline, or during follow-up from 1992-1999. On the basis of information from both surveys, the subjects were categorized as with or without a history of CVD. A history of diabetes was self-reported.

Educational level was self-reported and recorded in 6 categories: Not completed primary school, primary school (9 years), technical college (10-12 years), secondary school (10-12 years), and college or university less than 4 years and more than 4 years. Non-fasting EDTA blood samples were collected for the measurement of total homocysteine (tHcy), creatinine and gene polymorphisms. Plasma tHcy was measured by using a fully automated HPLC assay [26]. Apolipoprotein E (ApoE) ε4 genotypes were determined in the packed cell fraction of blood samples by using a one-stage polymerase chain reaction method [27]. Creatinine was measured in stored plasma by a modification of a liquid chromatography-mass spectrometry described previously [28].

The Hospital Anxiety and Depression Scale was used to assess depression (HADS-D) and anxiety (HADS-A) through a self administered questionnaire [29]. In this study, only the HADS-D score was used as it is more relevant to cognitive function [30]. When tested, HADS-A was not associated with vitamin D.

The smoking variable was coded as number of cigarettes smoked per day. Blood pressure was measured three times, and the variable used in this study is the average of the second and third measurement.

Age is not included due to the narrow age span of the participants.

Statistical Analyses

All calculations were performed by using SPSS 16.0 (SPSS INC, Chicago IL) unless otherwise stated. Results are expressed as medians with 25th and 75th percentiles or means with standard deviations (SD). Pearson's chi-square test and Student's t-test were used to examine relationships between independent groups. For comparisons between intakes of vitamin D containing foods in users and non-users of cod liver oil ANOVA was used. Spearman's rho correlation coefficients were used to assess simple correlations. Multiple linear and logistic regression analyses were performed to examine relationships between intake of vitamin D (entered as quintiles) and the cognitive test scores adjusted for relevant covariates. In logistic regression analysis, categories of intake were chosen to examine whether a low intake would increase the risk of scoring poorly on a cognitive test using the highest quintile as reference (vitamin D intake $\geq$ 15.7 μg/d). A poor cognitive test score was set to the ~10th percentile for all the tests, except for the TMT-A, where the 90th percentile was used [31]. To avoid over-adjustment, three regression models were routinely used; first adjusting for sex only, then two with multiple adjustments. When adjusting for potential confounders, we adjusted only for recognized determinants of cognitive function (e.g. education, ApoE ε4 allele status) or for variables that were significantly associated with 4 or more of the cognitive tests (including sum Z-score) as well as vitamin D intake in our data set. In the second model, which is presented in the text throughout the paper, the following variables were included: sex (men or women), education (6 categories), ApoE variant ε4 allele (presence or not presence), tHcy (quintiles), and total energy intake (quintiles). The third model included also nutritional covariates (quintiles) in addition to the aforementioned variables: intakes of fruits, cereals, meat and meat products, vegetables, sweets, tea, and wine. We assessed the association between month of cognitive testing and the cognitive scores. For several of the tests, we found the lowest score in

August and September. However, adjusting for this variable did not change the results and it was omitted from the analyses.

We have previously shown in this cohort that intake of both fatty fish and lean fish is associated with improved cognition [31]. In our population, cod liver oil provided a unique source of vitamin D. We therefore further explored the relationship between cognition (KOLT), lean fish and fatty fish by splitting the population into users and non-users of cod-liver oil. In a logistic regression analysis, the cognition variable was entered as dependent variable (dichotomous, 10th percentile as cut-off) and intake of lean fish (4 categories: 0, 0.1 – 25.0, 25.1 – 50.0 and ≥ 50.1 g/d) and fatty fish (4 categories: 0, 0.1 – 10.0, 10.1 – 20.0 and ≥ 20.1 g/d) was entered as indicator variables. For both types of fish, the highest intake group was used as reference. In addition to adjust for lean fish and fatty fish mutually, we also adjusted for sex, education, ApoE ε4 variant allele, tHcy and total energy intake. The same analysis was also conducted but including cod liver oil (0, 0.1 – 2.5, ≥ 2.6 g/d) as indicator variable, instead of using it as a selection variable.

All P-values are 2-sided, and values < 0.05 were considered significant.

RESULTS

Subject Characteristics, cognitive performance and dietary intake

The total number of participants included was 1916 (883 men and 1033 women), all born within the timeframe 1925-1927. The intake of vitamin D in the present population ranged from 0.5 to 56.1 µg/d, with a median of 7.3 µg/d (25th and 75th percentiles: 4.1,13.9). Sixty-four percent of the population did not meet the Nordic recommendations of vitamin D intake (≥10 µg/d) [32]. When defining a low cognitive test score as the tenth percentile (90th for the TMT-A), only 3 subjects were defined as scoring poorly on all of the cognitive tests, whereas 678 participants (35.4%) scored poorly on at least one test.

Comparisons of adequate vs. low intake of vitamin D

More men than women were significantly classified as having an adequate intake of vitamin D, i.e., ≥10 µg/d (**Table 1**). The educational level as well as total energy intake was significantly higher in the adequate intake group compared to the low intake group. Three of the cognitive tests (COWAT, m-DST, m-MMSE) and the Z-score were significantly higher in the adequate intake group compared to the low intake group. Plasma tHcy was significantly higher in the low intake group. Plasma creatinine was borderline significantly higher in the adequate intake group. There was no significant difference in smoking status, BMI, blood pressure, CVD or diabetes history or ApoE ε4 variant allele profile when comparing the two intake groups.

Dietary sources of vitamin D

Table 2 shows the contribution of vitamin D from the most important sources of vitamin D in the total population. Fish was the main contributor of vitamin D, with fatty fish as the most important source within the fish group. Fortified butter/margarines were the second most important source. Supplements were also an important contributor of vitamin D, with cod liver oil as the main

provider. Thus, dietary vitamin D derived mainly from fish, fortified butter/margarines and supplements, with these three products providing 93.2 % of total vitamin D intake. When we separated the group into users and non-users of cod liver oil, it became apparent that for the non-users, fish (total intake) contributed mostly to the total vitamin D intake with 46.4 (SD: 24.0) %, but that for the cod liver oil users, the cod liver oil was the most important source contributing with 50.8 (SD: 25.7) % (Table 1S). Also, for those taking cod liver oil as a supplement, the contribution of vitamin D from butter/margarines was much lower than for the non-user group (Table 1S).

Covariates associated with cognition and vitamin D

Associations between relevant dichotomous variables, cognitive test scores and vitamin D intake are presented in Table 2S. Men scored significantly better on the TMT-A and women scored better on the KOLT. No other tests differed according to sex. Men had a higher intake of vitamin D than women. ApoE ε4 variant allele was associated with significantly lower test scores for KOLT, m-MMSE, m-DST and Z-score. Vitamin D intake was not significantly associated with ApoE ε4 variant allele profile. The COWAT, KOLT and Z-score were significantly poorer for those with a history of CVD. The COWAT, KOLT, m-DST and Z-score were significantly higher for the subjects without diabetes. Because CVD and diabetes were not significantly associated with vitamin D, these variables were not included in the final analyses.

Spearman's Rho correlation coefficients between continuous variables, the cognitive tests and vitamin D intake are shown as supplemental data Table 3S. Vitamin D intake was correlated with COWAT, m-DST, m-MMSE, TMT-A and sum Z-score in addition to education, tHcy, creatinine, total energy intake and all of the food groups. At least four of the cognitive tests including sum Z-score were significantly associated with the following variables: Education, intake of total energy, depression score, vitamin D containing supplements, fish total (including all fish and fish products), lean fish, fatty fish, dairy products, fruit, meat and meat products, cereals, vegetables, sweets and

drinks (tea and wine). Coffee consumption was not correlated with vitamin D intake (data not shown). Among the nutritional variables, fruit, meat and meat products, cereals, vegetables, sweets and drinks did not contain vitamin D and were considered potential confounders. Smoking, blood pressure, HADS-D score, creatinine and BMI were associated with less than four of the cognitive tests and/or not associated with vitamin D and were therefore not included in further analyses.

Linear regression analyses

Linear regression analyses adjusted for sex indicated that a significant association between quintiles of vitamin D intake as independent variable and the COWAT, KOLT, m-DST, m-MMSE or the sum Z-score as dependent variable existed (**Table 3**). After additional adjustment with ApoE ε4 variant allele, education, tHcy, and energy intake, the COWAT and KOLT remained significantly associated with intake of vitamin D (Table 3). The association was markedly reduced compared to the sex-adjusted model, and it appeared that it was inclusion of education and total energy intake that accounted for the weakening of the association. In the final model, including adjustment for nutrients, none of the cognitive tests remained significant.

Risk of poor cognitive test performance according to intake of vitamin D

Using logistic regression, we first investigated the risk of scoring poorly on a cognitive test according to quintiles of total vitamin D intake. The upper quintile of vitamin D was used as the reference category.

In the model adjusted only for sex, when comparing the highest and lowest quintiles of vitamin D intake, there was an increase in risk for scoring poorly on the KOLT (OR = 1.74, 95 % CI: 1.08, 2.08), m-DST (OR = 1.90, 95 % CI: 1.11, 3.26), m-MMSE (OR = 1.40, 95 % CI: 0.84, 2.32), and the sum Z-score (OR = 1.74, 95 % CI:1.07, 2.83) , Ptrend < 0.05 for all.

In the multiple adjusted model, none of the tests remained significant (**Table 4**). However, those with vitamin D intake in the lowest quintile had significant increased odds ratio for scoring poorly on KOLT (OR = 1.81, 95 % CI: 1.04, 3.15). Further adjusting for additional nutrients marginally weakened the results (OR = 1.65, 95 % CI: 0.94, 2.89).

Sources of vitamin D vs. lean fish

As previously mentioned, an earlier study conducted on this cohort revealed an association between lean fish intake and the KOLT [31]. In the present study, we found that the KOLT was the only cognitive test that was significantly associated with vitamin D intake in both linear and logistic regression analyses in Model 2. The mean intakes of vitamin D, lean fish, fatty fish and fish total were all significantly higher in the user group of cod liver oil compared non-users (all P-values <0.001) (Table 1S). The amounts in grams however do not differ to a large extent, but the values become significant as a result of our large sample size. Among non-users of cod liver oil, the risk of scoring poorly on the KOLT increased when the intake of lean fish was low (0.1 g/d – 25.0 g/d, P = 0.027). When further adjusted for butter/margarines and other kinds of fish and fish products, the model weakened, but the same intake category for lean fish (0.1 – 25.0 g/d) stayed significant (OR = 1.82, 95 % CI: 1.01, 3.28, Ptrend = 0.030). No significant relationship was found when the same analysis was performed with fatty fish. We also tested for interaction between cod liver oil and fish intake: there was no significant interaction for fatty fish, but a borderline association for lean fish (P=0.072). When including cod liver oil in the model as an indicator variable, the risk of scoring poorly on the KOLT in fully adjusted model, low intake of lean fish was almost significant (0.1 – 25.0 g/d, OR = 1.57, 95 % CI: 0.99, 2.49, P = 0.054), whereas cod liver oil intake and fatty fish intake were not significantly associated.

DISCUSSION

In a large population-based study of elderly people living at high latitudes in a rainy climate, we found a significant association between vitamin D intake and cognitive test scores in several of the cognitive tests in the test battery (COWAT, KOLT, m-DST and Z-score). Furthermore, we found that the risk of scoring poorly on several cognitive tests increased when the vitamin D intake was low. However, adjustment for relevant covariates markedly reduced the strength of the association. In addition, we found that for non-users of cod liver oil, the risk of scoring poorly on the KOLT was associated with low intake of lean fish, while fatty fish, a rich source of vitamin D, did not contribute significantly.

Intake of vitamin D and current recommendations

The vitamin D intake in the present population showed a wide range (0.5 to 56.1 μg/d). If we use the Nordic Recommendations, 64.0% were defined as having a low intake of vitamin D. According to the American Recommendations for this age group, which is ≥15.0 μg/d [33], 77.6 % would be defined as having a low intake with only 22.4% having an adequate intake. Our population consumed high amounts of vitamin D containing foods such as cod liver oil and fish and fish products compared to other studies [34, 35]. O'Donnel et al found in their meta-analysis reviewing 11 randomised controlled trials that vitamin D fortified foods improved vitamin D status in adults in the United States. Data from NHANES 1999-2000 showed that total vitamin D intake from food sources across all age groups ranged from 3.8 – 6.9 μg/d, and that few older adults achieve recommended vitamin D intakes [36]. Furthermore, fortified foods provided 65 – 86 % of the total daily vitamin D intake from foods [13]. The United States fortify several foods such as orange juice, milk and yoghurt, margarine, flours and ready-to-eat breakfast cereals, and yet the intake is still much lower than the recommended daily allowance (RDA) [37]. Even though our population have a high intake of vitamin D containing foods and supplements, the majority were defined as having a

less than adequate intake. This would indicate that reaching the RDA is difficult, and measures need to be taken to ensure an adequate intake in the population. We found that for those not taking cod liver oil, fortified foods (butter and margarine) was an important source of vitamin D. The use of fortification and supplements together will probably be required. Mosekilde speculate that one of the reasons as to why serum levels in the USA have a higher range than Europe [38] is because of the liberal fortification politics in Northern America compared to Europe [39].

Intake of vitamin D and cognitive test performance

We found that a low intake of vitamin D increased the risk of scoring poorly on several of the cognitive tests (COWAT, KOLT, m-DST, m-MMSE and sum Z-scores). However, after multiple adjustments, only the KOLT (episodic memory) and COWAT (semantic memory) remained significant but weaker in linear associations. None of the tests were significant when the risk for poor test performance was assessed. Several studies have shown an association with vitamin D in serum and cognitive decline [6, 40, 41], these are, however, observational studies, and so far evidence based on randomized clinical trials is lacking. Furthermore, some studies have found no relationship between serum vitamin D concentrations and cognition [42, 43]. A review article by Annweiler et al reviewed 5 cross sectional studies that had looked into the relationship between serum 25(OH)D and cognition [44]. They found the evidence to be inconclusive.

Fatty fish, lean fish, cod liver oil and cognitive performance

The best sources of vitamin D in our study were fatty fish and cod liver oil. These products contain not only vitamin D, but a number of other important nutrients that have been associated with cognition, essential fatty acids being among them [45]. Studies have come up with conflicting results when it comes to the intake of essential fatty acids, fish intake and cognition [46-48]. Dangour et al were not able to show any protective effect of fish oil supplements in their

randomised controlled trial. The trial only ran for 24 months and so it was speculated that the intervention period was too short to show any effect [49]. Devore et al found, using data from the Rotterdam study that a moderate consumption of fish and omega-3 polyunsaturated fatty acids (PUFAs) were not associated with long term risk of dementia, and that there were little or no difference if the subjects typically consumed fatty fish, lean fish or omega-3 PUFAs [48].

In theory, if vitamin D is protective of cognitive decline, vitamin D containing foods would also have a protective effect on cognition. We found that the food items that contribute substantially to the total intake of vitamin D were cod liver oil, fatty fish, and butter and margarines. Also, the intake of lean fish was very high in the present population. Interestingly, a high intake of lean fish, which is not high in vitamin D, was more strongly associated with cognitive performance than fatty fish and cod liver oil.

A diet rich in fish might be a part of other lifestyle choices and a dietary pattern that is protective of cognitive decline [50]. Furthermore, a diet high in fish and fish products may replace other unhealthy nutrients such as saturated fatty acids from meat. And indeed, studies have found that a dietary pattern that resembles the Mediterranean diet, which is high in fish, vegetables, fruits and nuts, olive oil (mono unsaturated fatty acids), cereals, low in meat and dairy products, and moderate consumption of alcohol, might be protective of cognitive decline [50].

Strengths and limitations

The strengths of this study are the large number of participants as well as an extensive battery of cognitive tests. The large test battery made it possible to test which aspects of cognition that might be more affected than others. Because 71% of the study participants volunteered for cognitive testing, recruitment bias may have been an issue. Several differences between those who underwent and who did not undergo cognitive testing were reported earlier [51]. However, the dietary habits

were similar, and the intake of vitamin D was to a large extent the same. In this study we have used data that gives an estimated intake of vitamin D calculated from a self-administered FFQ. The FFQ has been validated in several studies [24, 25], however not with serum vitamin D as a biomarker. People suffering from cognitive ailments might have changed their diet as a result of the disease, and self reported dietary data collected from people who are cognitively impaired may be less reliable. However, because these were free-living subjects and the vast majority were not impaired, we do not think this had major impact on our findings.

Conclusion

In a population-based cross-sectional study, we found weak associations between vitamin D intake from foods and supplements, and cognitive performance. Also, we found that for non-users of cod liver oil, a low intake of lean fish was associated with having an increased risk of scoring poorly on the KOLT (episodic memory), whereas a low intake of fatty fish had no risk associated with it. It remains unclear whether it is vitamin D itself, food items or dietary pattern that is protective when it comes to cognitive performance. Future studies exploring the relationship between cognition and dietary pattern are certainly warranted.

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Table 1. Characteristics

		Adequate (≥ 10 µg)		Low (< 10 µg)	
	n	n (%) or mean (SD)	*n*	n (%) or mean (SD)	P-value[1]
Sex (male)	690	393 (57.0)	1226	490 (40.0)	<0.001
Education ≤9 y	651	205 (31.5)	1128	460 (40.8)	<0.001
Daily smoker (yes)	690	91 (13.2)	1225	156 (12.7)	0.866
Number of cigarettes/d amongst smokers	91	9.5 (4.5)	156	10.6 (7.9)	0.638
BMI	690	25.9 (3.7)	1223	26.2 (4.0)	0.182
Total energy (kJ)	690	8671 (2272)	1226	6964 (2062)	<0.001
Vitamin D (µg/d)	690	18.8 (7.6)	1226	5.1 (2.4)	<0.001

Systolic blood pressure	690	146 (21)	1226	146 (20)	0.928
Diastolic blood pressure	690	78 (12)	1226	77 (12)	0.160
History of CVD (yes)	677	216 (31.9)	1192	411 (34.5)	0.279
Diabetes (yes)	678	39 (5.8)	1211	85 (7.5)	0.332
Depression score	664	3.3 (2.7)	1129	3.6 (2.8)	0.085
Cognitive test scores					
COWAT	690	15.0 (5.3)	1226	15.8 (5.7)	0.001
KOLT	690	35.2 (8.2)	1226	35.8 (7.6)	0.097
m-DST	690	10.2 (4.2)	1226	10.8 (4.3)	0.002
m-MMSE	690	11.5 (0.8)	1226	11.6 (0.7)	0.047
TMT-A	690	57 (33)	1226	54 (32)	0.074
m-BD	690	15.1 (2.2)	1226	15.1 (2.1)	0.692

Z-score	690	0.96 (0.98)	1226	-0.05 (1.01)	0.002
Plasma variables and ApoE ε4 variant allele status					
tHcy (µmol/L)	690	11.7 (3.6)	1221	12.1 (3.9)	0.027
Creatinine (µmol/L)	690	78.3 (19.4)	1219	76.4 (18.6)	0.053
ApoE (ε4 variant allele present)					
	686	214 (31.2)	1216	392 (32.2)	0.645

[1] Pearson X^2- test with continuity correction or Students *t*-test

Table 2. Mean and median intakes of vitamin D from different food groups, as well as the relative contribution of vitamin D intake from the different food groups in the total population.

	Total population (n = 1916)		
	Mean (SD)	Median (25th and 75th percentile)	Mean percent contribution (SD)
Supplements total			
Total intake (g/d)	2.1 (3.5)	0 (0, 2.8)	
Vitamin D (µg/d)	4.2 (7.1)	0 (0, 6.05)	23.4 (31.3)
Cod liver oil			
Total intake (g/d)	1.7 (3.0)	0 (0, 2.0)	
Vitamin D (µg/d)	3.6 (6.5)	0 (0, 4.3)	18.8 (29.1)
Supplements rest			

Total intake (g/d)	0.4 (1.6)	0 (0, 0)	
Vitamin D (µg/d)	0.6 (2.1)	0 (0, 0)	4.6 (13.9)
Fish total			
Total food intake (g/d)	88.6 (55.5)	80.3 (49.6, 116)	
Vitamin D (µg/d)	3.4 (3.2)	2.5 (1.1, 4.6)	38.3 (24.4)
Fish fatty			
Total food intake (g/d)	14.7 (16.9)	9.3 (2.4, 20.9)	
Vitamin D (µg/d)	2.1 (2.4)	1.3 (0.4, 3.1)	22.8 (20.9)
Fish lean			
Total food intake (g/d)	36.6 (29.4)	29.7 (15.0, 50.5)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)	3.2 (3.6)
Fish rest			
Total food intake (g/d)	37.7 (29.2)	32.4 (18.3, 49.2)	

Vitamin D (µg/d)	1.1 (1.4)	0.7 (0.1, 1.5)	12.3 (13.2)
Butter[1]			
Total food intake (g/d)	26.1 (17.3)	23.4 (13.1, 35.3)	
Vitamin D (µg/d)	2.0 (1.2)	1.8 (1.1, 2.7)	31.5 (22.0)
Eggs			
Total food intake (g/d)	15.8 (11.5)	15.3 (7.7, 19.4)	
Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)	3.9 (5.0)
Dairy products[2]			
Total food intake (g/d)	343 (206)	321 (195, 458)	
Vitamin D (µg/d)	0.1 (0.1)	0.1(0.1, 0.2)	2.4 (7.1)

[1] Includes butter/margarines from fried vegetables, potatoes and baking

[2] Includes milk and milk products and cheese

Table 3. Linear regression analyses

	Partial r^1	*P*-value[1]	Partal r^2	P-value[2]
COWAT	0.114	<0.001	0.055	0.021
KOLT	0.077	0.001	0.049	0.041
m-DST	0.079	0.001	0.00	0.930
m-MMSE	0.052	0.022	0.01	0.649
TMT-A	-0.02	0.304	0.02	0.493
m-BD	0.04	0.075	0.00	0.857
Z-scores	0.103	<0.001	0.03	0.246

[1] Adjusted for sex

[2] Adjusted for sex, ApoE ε4 variant allele, education, tHcy and total energy

Table 4. Risk for poor cognitive performance by quintiles of vitamin D intake

	n = 1761	Intake of vitamin D by quintiles	OR[1]	95% CI for OR
COWAT				
	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.68	0.39, 1.16
	358	5.96 - 9.19	0.74	0.43, 1.28
	360	3.58 - 5.95	0.94	0.56, 1.59
	322	≤ 3.57	1.10	0.73, 2.29
***P*-trend**			0.318	
KOLT				
	365	≥ 15.63	*ref*	

	356	9.20 - 15.62	0.89	0.52, 1.48
	358	5.96 - 9.19	1.00	0.59, 1.68
	360	3.58 - 5.95	0.71	0.41, 1.26
	322	≤ 3.57	1.81	1.04, 3.15
***P*-trend**			0.161	
m-DST				
	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.76	0.38, 1.50
	358	5.96 - 9.19	1.31	0.70, 2.45
	360	3.58 - 5.95	1.27	0.68, 2.37
	322	≤ 3.57	1.55	0.79, 3.05
***P*-trend**			0.092	
m-MMSE				

	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.39	0.19, 0.79
	358	5.96 - 9.19	0.95	0.54, 1.67
	360	3.58 - 5.95	0.94	0.54, 1.66
	322	≤ 3.57	0.88	0.47, 1.64
***P*-trend**			0.609	
TMT-A				
	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.79	0.46, 1.36
	358	5.96 - 9.19	1.20	0.73, 2.00
	360	3.58 - 5.95	0.91	0.53, 1.54
	322	≤ 3.57	0.78	0.43, 1.41
***P*-trend**			0.636	

m-BD				
	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.83	0.53, 1.31
	358	5.96 - 9.19	0.80	0.50, 1.26
	360	3.58 - 5.95	0.74	0.46, 1.17
	322	≤ 3.57	0.94	0.58, 1.53
***P*-trend**			0.605	
Z-scores				
	365	≥ 15.63	*ref*	
	356	9.20 - 15.62	0.96	0.55, 1.67
	358	5.96 - 9.19	1.19	0.69, 2.05
	360	3.58 - 5.95	0.94	0.53, 1.65
	322	≤ 3.57	1.31	0.72, 2.37

***P*-trend**	0.477

[1] Adjusted for sex, ApoE ε4 variant allele, education, tHcy and total energy intake

Table 5. Binomial logistic regression analysis showing risk of scoring poorly on the KOLT as a result of decreased intake of lean and fatty fish with the population divided into users/non-users of cod liver oil.

			User (*n* = 672)			Non-user (*n* = 1089)	
		n	OR	95% CI	*n*	OR	95% CI
KOLT							
Lean Fish	≥ 50.1 g/d	198	*ref*		270	*ref*	
	25.1 - 50.0 g/d	242	0.76	0.36, 1.60	385	0.98	0.55, 1.74
	0.1 - 25.0 g/d	194	1.23	0.57, 2.63	345	1.92	1.08, 3.43
	0.0 g/d	38	0.71	0.15, 3.44	89	1.82	0.83, 3.99
P-trend[1]			0.845			0.016	
Fatty Fish	≥ 20.1 g/d	204	*ref*		266	*ref*	

	10.1 - 20.0 g/d	165	0.74	0.77, 3.95	235	0.74	0.40, 1.38
	0.1 - 10.0 g/d	216	1.47	0.64, 3.38	368	0.90	0.52, 1.57
	0.0 g/d	87	1.87	0.69, 5.04	220	1.06	0.58, 1.69
P-trend[1]			0.255			0.743	

[1] Adjusted for sex, ApoE ε4 variant allele, education, plasma tHcy, total energy intake and mutually for fatty or lean fish intake

Table 1S. Mean and median intakes of vitamin D from different food groups stratified by intake of cod liver oil, and the relative contribution of vitamin D intake from the different food groups.

	Non-user (n = 1206)			**User (n = 710)**		
	Mean (SD)	**Median** (25th and 75th percentiles)	**Mean percent contribution** (SD)	**Mean (SD)**	**Median** (25th and 75th percentiles)	**Mean percent contribution (SD)**

Vitamin D total (µg/d)		6.0 (4.1)	5.2 (3.1, 7.8)		17.0 (8.9) [3]	15.5 (10.1, 23.9)	
Supplements total				4.4 (14.7)			55.7 (24.8)
	Total intake (g/d)	0.3 (1.4)	0 (0, 0)		5.0 (4.1)[3]	5.1 (1.7, 6.5)	
	Vitamin D (µg/d)	0.4 (1.6)	0 (0, 0)		10.6 (8.1)	11.0 (4.1, 15.1)	
Cod liver oil				–			50.8 (25.7)
	Total intake (g/d)	–	–		4.5 (3.5)	5.1 (1.4, 5.6)	
	Vitamin D (µg/d)	–	–		9.7 (7.5)	11.0 (3.0, 12.1)	
Supplements rest				4.4 (14.7)			4.9 (12.3)
	Food intake (g/d)	0.3 (1.4)	0 (0, 0)		0.5 (1.9)[4]	0 (0, 0)	
	Vitamin D (µg/d)	0.4 (1.6)	0 (0, 0)		0.9 (2.6)	0 (0, 0)	
Fish total				46.4 (24.0)			24.7 (18.3)
	Food intake (g/d)	83.2 (52.9)	74.9 (44.9, 111)		98.7 (58.3)[3]	90.6 (59.2, 125)	
	Vitamin D (µg/d)	3.1 (3.1)	2.3 (1.0, 4.2)		3.8 (3.3)	2.9 (1.4, 5.2)	

Fatty fish				27.4 (22.7)			14.9 (14.3)
	Food intake (g/d)	13.6 (16.7)	8.2 (2.1, 19.4)		16.6 (16.9)[3]	11.3 (3.5, 24.0)	
	Vitamin D (µg/d)	1.9 (2.4)	1.2 (0.3, 2.8)		2.4 (2.4)	1.6 (0.5, 3.4)	
Lean fish				4.1 (4.08)			1.8 (1.8)
	Food intake (g/d)	34.4 (27.5)	27.5 (15.0, 48.9)		40.3 (32.0)[3]	34.1 (17.8, 53.8)	
	Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)		0.2 (0.2)	0.2 (0.1, 0.3)	
Fish rest				14.9 (14.6)			8.0 (8.9)
	Food intake (g/d)	35.2 (27.7)	30.3 (16.0, 46.9)		41.9 (31.1)[3]	36.5 (23.0, 52.9)	
	Vitamin D (µg/d)	1.0 (1.4)	0.5 (0.1, 1.4)		1.2 (1.6)	0.8 (0.2, 1.7)	
Butter/margarines[1]				40.3 (21.4)			16.6 (13.2)
	Food intake (g/d)	55.9 (37.5)	48.1 (28.4, 75.2)		63.9 (37.8)[3]	57.9 (36.0, 81.8)	
	Vitamin D (µg/d)	1.7 (1.1)	1.5 (0.9, 2.4)		1.8 (1.2)	1.6 (0.8, 2.5)	
Egg				5.3 (5.7)			1.7 (1.7)

	Food intake (g/d)	16.0 (11.9)	15.3 (7.7, 19.4)		15.4 (10.8)[4]	15.4 (7.7, 19.4)
	Vitamin D (µg/d)	0.2 (0.2)	0.2 (0.1, 0.3)		0.2 (0.2)	0.2 (0.1, 0.3)
Dairy products[2]				3.2 (3.5)		1.1 (1.1)
	Food intake (g/d)	328 (203)	301 (180, 435)		367 (208)[3]	346 (217, 485)
	Vitamin D (µg/d)	0.1 (0.1)	0.1 (0.1, 0.1)		0.1 (0.1)	0.1 (0.1, 0.2)

[1] Includes butter/margarines from fried vegetables, potatoes and baking

[2] Includes milk and milk products and cheese

[3] ANOVA adjusted for sex. Significant at P<0.001

[4] ANOVA adjusted for sex. Not significant

Table 2S. Student's T-test on dichotomous variables in reference to cognitive test scores and vitamin D intake

	Sex		ApoE		CVD		Diabetes	
	Mean difference[1]	*P*-value[3]	Mean difference[2]	*P*-value	Mean difference[2]	*P*-value	Mean difference[2]	*P*-value
COWAT	-0.04	0.862	-0.25	0.347	-0.57	0.035	-1.72	0.001
KOLT	-3.19	<0.001	-1.19	0.002	-1.67	<0.001	-1.66	0.024
m-DST	0.15	0.44	-0.52	0.012	-0.21	0.323	-0.91	0.021
m-MMSE	0.03	0.32	-0.1	0.011	-0.05	0.184	-0.1	0.132
TMT-A	-3.47	0.019	3.19	0.055	3.05	0.057	3.13	0.299
m-BD	0.14	0.16	-0.03	0.776	-0.12	0.261	-0.2	0.327
Z-score	-0.06	0.171	-0.13	0.007	-0.16	0.001	-0.29	0.002
Vitamin D	2.96	<0.001	0.25	0.529	-0.09	0.821	-0.53	0.493

[1] Men - women

[2] Sick - healthy

[3] *P*-value from Student's *t*-test

Table 3S. Simple correlations between continuous covariates, the cognitive tests and vitamin D intake

	n	COWAT	KOLT	m-DST	m-MMSE	TMT-A	m-BD	Z-score	Vitamin D
Vitamin D	1916	0.12**	0.03	0.08**	0.05*	-0.05*	0.04	0.10**	1.000
Education	1779	0.33**	0.11**	0.42**	0.20**	-0.27**	0.17**	0.40**	0.15**
tHcy	1911	-0.06**	-0.14**	-0.06*	-0.04	0.07**	-0.02	-0.11**	-0.05*
BMI	1913	-0.05*	-0.05*	-0.03	-0.02	-0.02	-0.02	-0.05*	-0.04
Depression score	1793	-0.06*	-0.10**	-0.10**	-0.01	0.10**	-0.04	-0.12**	-0.03
Smoking	1916	0.00	-0.01	-0.03	-0.02	0.07**	-0.07**	-0.05*	0.03
Creatinine	1909	0.03	-0.10**	0.01	0.03	-0.05*	0.05*	0.00	0.09*
Systolic blood pressure	1916	-0.051*	0.006	-0.036	-0.047*	0.014	0.005	-0.031	-0.013
Diastolic blood pressure	1916	-0.032	-0.023	-0.015	-0.002	-0.039	0.021	0.000	0.048*

Total energy	1916	0.06*	-0.03	0.06*	0.04	-0.01	0.05*	0.05*	0.48**
Supplements	1916	0.12**	0.05*	0.07**	0.04	-0.05*	0.04	0.10**	0.75**
Fish	1916	0.05*	0.05*	0.07**	0.07**	-0.07**	0.07**	0.09**	0.53**
Fatty	1916	0.06**	0.06**	0.06**	0.03	-0.06**	0.03	0.08**	0.50**
Lean and medium	1916	0.02	0.06**	0.04	0.08**	-0.05*	0.06*	0.07**	0.29**
Butter/oils[1]	1916	0.02	-0.05	0.06**	0.04	-0.04	0.07**	0.05*	0.35**
Eggs	1916	-0.00	0.0.3	-0.05*	0.02	0.01	-0.02	-0.04	0.12**
Dairy products[2]	1916	-0.05*	-0.02	-0.09**	-0.02	0.08**	0.02	-0.07**	0.14**
Fruit[3]	1916	0.13**	0.12**	0.14**	0.08**	-0.09**	0.10**	0.18**	0.23**
Meat and meat products	1916	0.06**	0.01	0.07**	0.07**	-0.03	0.07**	0.07**	0.31**
Cereals[4]	1916	0.07**	0.03	0.09**	0.05*	-0.10**	0.11**	0.11**	0.22**

Vegetables[5]	1916	0.11**	0.09**	0.112**	0.11**	-0.09**	0.05*	0.15**	0.25**
Sweets	1916	0.09**	0.04	0.10**	0.02	-0.05*	0.07**	0.11**	0.15**
Drinks									
Tea	1916	0.10**	0.09**	0.13**	0.09**	-0.11**	0.05*	0.16**	0.06*
Wine	1916	0.23**	0.14**	0.23**	0.15**	-0.17**	0.09**	0.27**	0.16**

* P<0.05

** P<0.001

[1] Butter/margarines including from baking and fried onions and fried potatoes

[2] Dairy products including milk and milk products and cheese

[3] Fruit + juice

[4] Cereals with pizza extracted

[5] Vegetables with fried onions extracted

Appendices

Appendix I	Consent form
Appendix II	Hordaland Health Study; questionnaire 1
Appendix III	Invitation letter
Appendix IV	Hordaland Health Study; food frequency questionnaire
Appendix V	Hordaland Health Study; cognitive testing
Appendix VI	Hospital Anxiety and Depression Scale

HORDALANDSUNDERSØKELSEN '97 - '99 (HUSK)

SAMTYKKEERKLÆRING

I brosjyren "HUSK" er jeg orientert om Hordalands-undersøkelsens formål. Jeg har også sett informasjonsskrivet "HUSK INFO" som bl.a. omtaler delprosjekter, og er kjent med at undersøkelsen består av spørreskjema, blodprøve og måling av blodtrykk, høyde, vekt, liv- og hoftevidde.

Jeg er kjent med at opplysninger om meg blir behandlet strengt fortrolig og at undersøkelsen er vurdert og tilrådd av Den regionale komité for medisinsk forskningsetikk og godkjent av Datatilsynet. Det er ikke satt noen spesiell tidsbegrensning for hvor lenge opplysningene kan lagres, men jeg er klar over at jeg på hvilket som helst tidspunkt kan trekke meg fra undersøkelsen og kan reservere meg mot bruk av opplysninger om meg.

1. Jeg samtykker i at resultater fra blodprøven og andre deler av undersøkelsen, samt resultater fra eventuelle spesialundersøkelser, blir sendt til den legen jeg har oppgitt på spørreskjemaet.

2. Dersom jeg ikke har oppgitt navn på lege, eller legen min ikke deltar i undersøkelsen, samtykker jeg i at mine resultater sendes til kommunelege I.

3. Jeg samtykker i at jeg kan få tilbud om spesialundersøkelser, og at jeg kan bli kontaktet av en lege med tanke på tilbud om behandling eller for å forebygge sykdom.

4. Jeg samtykker i at mine resultater kan brukes til medisinsk forskning, eventuelt ved å sammenholde opplysninger om meg med opplysninger fra andre helse-, trygde- og sykdomsregistre, eller med mine resultater fra tidligere helseundersøkelser i Hordaland. Når disse opplysningene sammenholdes, vil mitt navn og personnummer ikke bli tatt med.

5. Jeg samtykker i at blodprøve oppbevares. All bruk av denne vil bare skje etter godkjenning fra Datatilsynet og Den regional komité for medisinsk forskningsetikk.

Vennligst stryk det/de avsnitt du reserverer deg mot.

....

Sted og dato Underskrift

FRAMMØTE DATO

Sykepl. kode BT 84

DAG MND. ÅR 17

HØYDE

VEKT

H/V 25

ANM.

AVVIK BT-MÅL.

ARM OMKR.

MANSJ. STØRR.

AP.NR

TSM 32

KOMMUNE 85-88

MÅLING 1

MAP 35

S 38

HR 53

D 56

MÅLING 2

MAP 41

S 44

HR 59

D 62

MÅLING 3

MAP 47

S 50

HR 65

D 68

SAMTYKKE
Tilhørende hjerte-kar.

JA/NEI

1 2 3 4 5 74

SAMTYKKE
Kvinneutvalg

JA/NEI 75

OMKRETS

MIDJE 78

HOFTE 81

Sykepl. kode blod-prøve

(ID-1/97) 30.000. 10-97. e.s.trykk

Hvor ofte i løpet av de siste 4 ukene har du hatt mye overskudd? Sett bare ett kryss.

	JA
Hele tiden	1
Nesten hele tiden	2
Mye av tiden	3
En del av tiden	4
Litt av tiden	5
Ikke i det hele tatt	6

Hvor ofte i løpet av de siste 4 ukene har du følt deg nedfor og trist? Sett bare ett kryss.

	JA
Hele tiden	1
Nesten hele tiden	2
Mye av tiden	3
En del av tiden	4
Litt av tiden	5
Ikke i det hele tatt	6

I løpet av de siste 4 ukene, hvor mye av tiden har din fysiske helse eller følelsesmessige problemer påvirket din sosiale omgang(som det å besøke venner, slekt)? Sett bare ett kryss.

	JA
Hele tiden	1
Nesten hele tiden	2
Mye av tiden	3
En del av tiden	4
Litt av tiden	5
Ikke i det hele tatt	6

Stort sett, vil du si at din helse er:

Utmerket	Meget god	God	Nokså god	Dårlig
1	2	3	4	5

11. BRUK AV MEDISINER

Med medisiner mener vi her alle slags medisiner, både:
- *med og uten resept, naturmedisin, vitaminer og mineraler*
- *medisin som svelges, inhaleres eller injiseres, stikkpiller, salver, kremer eller dråper.*

Tok du noen slags medisiner I GÅR? JA NEI

Hvis NEI, kan du gå til avsnitt 12.
Hvis JA, besvar følgende:
Hvilke medisiner tok du I GÅR, og hva var grunnen til at du tok medisinen (diagnose, sykdom, symtom, helseeffekt)?
Sett svarene inn i skjemaet nedenfor, en linje for hver medisin.
Kryss av for ja om du bruker medisinen daglig eller nesten daglig.

Navn på medisinen *(ett navn pr. linje):*	Grunn til bruk av medisinen I GÅR var:	Daglig JA	Daglig NEI

Dersom det ikke er nok plass her, kan du fortsette på eget ark som legges ved.

12. ARBEID

Besvares av dem som har hatt inntektsgivende arbeid i minst 100 timer det siste året:
Beskriv virksomheten på det arbeidsstedet der du utførte inntektsgivende arbeid i lengst tid de siste 12 mnd. *(Skriv f.eks. jordbruk, barneavd. på sykehus, snekkeravd. på skipsverft e.l.).*

Virksomhet:

Hvilket yrke/tittel har eller hadde du på dette arbeidsstedet?
(Skriv f.eks. kornbonde, anestesisykepleier, snekker e.l.)

Yrke:

Hvor lenge har du praktisert i dette yrket i ditt liv? ..... *Antall år i yrket*

Har du noen av de følgende yrker (*heltid eller deltid*)?
Sett kryss for hvert spørsmål.

	JA	NEI
Sjåfør		
Bonde/gårdbruker		
Fisker		

Har du tidligere i ditt liv (*ikke i dag*) hatt inntektsgivende arbeid som:

	JA	NEI
Bilmekaniker/biloppretter		
Frisør		

13. SAMLIV

Oppgi antall egne barn (eventuelt 0) av hvert kjønn:

Antall gutter *Antall jenter*

Har du noen gang hatt regelmessig samliv uten prevensjon i ett år eller mer uten at det har ført til graviditet?... JA NEI
Med prevensjon menes også mer usikre metoder som avbrutt samleie, «sikre perioder» etc.

De følgende spørsmål besvares bare av kvinner

Har du noen gang spontanabortert (ufrivillig mistet fosteret) etter at graviditet var sikkert påvist?

NEI USIKKER JA

Hvis JA: *Antall ganger*

Følgende spørsmål besvares bare hvis du har vært gravid:
Oppgi antall måneder det tok med regelmessig samliv uten prevensjon (eller evt. amming), til du ble gravid:

Siste svangerskap ..... *mnd. uten prevensjon*

Nest siste svangerskap..... *mnd. uten prevensjon*

Tredje siste svangerskap ..... *mnd. uten prevensjon*

14. ETTERUNDERSØKELSE

Hvis denne helseundersøkelsen viser at du bør undersøkes nærmere, hvilken allmennpraktiserende lege/kommunelege ønsker

Ikke skriv i disse rutene

Takk for utfyllingen!
Nok en gang: *Velkommen til undersøkelsen*

IE 3215801 (ID.NR. 1.97): 30.000- Beyer-Hetos 9.97

HELSEUNDERSØKELSEN I HORDALAND 1997-99

Adresse endring

HUSK

Personlig innbydelse

Spørreskjemaet er en viktig del av helseundersøkelsen. Vennligst fyll ut skjemaet på forhånd og ta det med til helseundersøkelsen. Dersom enkelte spørsmål er uklare, lar du dem stå ubesvart til du møter fram, og drøfter dem med personalet som gjennomfører undersøkelsen. *Alle svar vil bli behandlet strengt fortrolig.*

Det utfylte skjemaet vil bli lest av en maskin. Bruk blå eller sort farge ved utfylling. Det er viktig at du går fram slik:

- i de små boksene setter du kryss for det svaret som passer best for deg
- i de store boksene skriver du tall eller blokkbokstaver – NB! innenfor rammen for boksen.

Eksempler:
Avkryssing: ☒ Tall: 1 2 3 4 5 6 7 8 9 0 Bokstaver: A B C

Med vennligh hilsen

Statens helseundersøkelser ♥ Kommunehelsetjenesten ♥ Helseundersøkelsen i Hordaland

1. EGEN HELSE

Hvordan er helsen din nå? *(Sett bare ett kryss)*

Dårlig	Ikke helt god	God	Svært god
☐ 1	☐ 2	☐ 3	☐ 4

Har du, eller har du hatt:	JA	NEI	Alder første gang	
Hjerteinfarkt	☐	☐		år
Angina pectoris (hjertekrampe)	☐	☐		år
Hjerneslag/hjerneblødning	☐	☐		år
Astma	☐	☐		år
Diabetes (sukkersyke)	☐	☐		år
Multippel sklerose	☐	☐		år

Bruker du medisin mot høyt blodtrykk?

Nå	Før, men ikke nå	Aldri brukt
☐ 1	☐ 2	☐ 3

Har du noen gang det siste året hatt eksem (rød, kløende, sår og sprukken hud):	JA	NEI
På hendene?	☐	☐
I ansiktet?	☐	☐
Andre steder på kroppen?	☐	☐

Med «hvite fingre» mener vi plager i form av at en eller flere fingre blir hvite og at man samtidig mister følelsen i dem når det er kaldt. Har du slike plager?	JA	NEI
	☐	☐

2. HVORDAN FØLER DU DEG?

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Nervøs og urolig?	☐ 1	☐ 2	☐ 3	☐ 4
Plaget av angst?	☐ 1	☐ 2	☐ 3	☐ 4
Trygg og rolig?	☐ 1	☐ 2	☐ 3	☐ 4
Irritabel?	☐ 1	☐ 2	☐ 3	☐ 4
Glad og optimistisk?	☐ 1	☐ 2	☐ 3	☐ 4
Nedfor/deprimert?	☐ 1	☐ 2	☐ 3	☐ 4
Ensom?	☐ 1	☐ 2	☐ 3	☐ 4

3. SYKDOM I FAMILIEN

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)?	JA	NEI	VET IKKE
	☐	☐	☐

Har en eller flere foreldre/søsken hatt:			
Hjerteinfarkt *før* de fylte 60 år?	☐	☐	☐
Hjerneslag/hjerneblødning *før* de fylte 70 år?	☐	☐	☐

4. MUSKEL- OG SKJELETTPLAGER

Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende?	JA	NEI
	☐	☐

Hvis NEI, gå til avsnitt 5.
Hvis JA, svar på følgende:

Hvor har du hatt disse plagene?	JA	NEI
Nakke	☐	☐
Skuldre (aksler)	☐	☐
Albuer	☐	☐
Håndledd/hender	☐	☐
Bryst, mage	☐	☐
Øvre del av ryggen	☐	☐
Korsryggen	☐	☐
Hofter	☐	☐
Knær	☐	☐
Ankler, føtter	☐	☐

Hvor lenge har plagene vart sammenhengende?
Svar for det området hvor plagene har vart lengst.

Hvis under 1 år, oppgi antall måneder. *Antall mnd.*

Hvis 1 år eller mer, oppgi antall år *Antall år*

Har plagene redusert din arbeidsevne det siste året?
Gjelder også hjemmearbeidende. Sett bare ett kryss.

Nei/ubetydelig	I noen grad	I betydelig grad	Vet ikke
☐ 1	☐ 2	☐ 3	☐ 4

Har du vært sykmeldt p.g.a. disse plagene det siste året?	JA	NEI	Ikke i arbeid
	☐	☐	☐

Har plagene ført til redusert aktivitet i fritiden?	JA	NEI
	☐	☐

5. MOSJON

Hvordan har din fysiske aktivitet i fritiden vært det siste året?
Tenk deg et ukentlig gjennomsnitt for året.
Arbeidsvei regnes som fritid. Besvar begge spørsmålene.

	Timer pr. uke			
	Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)*	☐ 1	☐ 2	☐ 3	☐ 4
Hard fysisk aktivitet *(svett/andpusten)*	☐ 1	☐ 2	☐ 3	☐ 4

6. KAFFE / TE / ALKOHOL

Hvor mange kopper kaffe/te drikker du daglig?
Sett 0 hvis du ikke drikker kaffe/te daglig.

Antall kopper daglig

Kokekaffe	Annen kaffe	Te

Er du total avholdsmann/-kvinne?	JA	NEI
	☐	☐

Hvor mange ganger i måneden drikker du vanligvis alkohol? *Regn ikke med lettøl.*
Sett 0 hvis mindre enn 1 gang i mnd.....Antall ganger

Hvor mange glass øl, vin eller brennevin drikker du VANLIGVIS i løpet av to uker?
Regn ikke med lettøl. Sett 0 hvis du ikke drikker alkohol.

Glass øl	Glass vin	Glass brennevin

7. RØYKING

Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?.....*Antall hele timer*
Sett 0 hvis du ikke oppholder deg i røykfylt rom.

Røyker du selv:	JA	NEI
Sigaretter daglig?	☐	☐
Sigarer/sigarillos daglig?	☐	☐
Pipe daglig?	☐	☐

Aldri røykt daglig ..... (Sett kryss) ☐

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet?.....*Antall år*

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig?.....*Antall sigaretter*

Hvor gammel var du da du begynte å røyke daglig? .....*Alder i år*

Hvor mange år til sammen har du røykt daglig? .....*Antall år*

8. ENDRING AV HELSEVANER

Dette gjelder din interesse for å endre helsevaner. Røykespørsmålet besvares bare av dem som røyker.

	Spise sunnere		Trimme mer		Slutte å røyke	
Har du de siste 12 mnd. forsøkt å:	JA	NEI	JA	NEI	JA	NEI
	☐	☐	☐	☐	☐	☐

Om 5 år, tror du at du har endret vaner på noen av disse områdene?	JA	NEI	JA	NEI	JA	NEI
	☐	☐	☐	☐	☐	☐

Anslå din høyeste og laveste vekt i løpet av de siste 5 år. *(Hele kg)* *(Se bort fra vekt under svangerskap)*	Høyeste vekt	Laveste vekt

9. UTDANNING

Hvilken utdanning er den høyeste du har fullført?
Sett bare ett kryss.

Mindre enn 7 år grunnskole	☐
Grunnskole 7-10 år, framhaldsskole, folkehøgskole	☐ 1
Realskole, middelskole, yrkesskole, 1-2 årig videregående skole	☐ 2
Artium, øk.gymnas, allmennfaglig retning i videregående skole	☐ 3
Høgskole/universitet, mindre enn 4 år	☐ 4
Høgskole/universitet, 4 år eller mer	☐ 5

10. HELSE OG TRIVSEL

De neste spørsmålene handler om hvordan du ser på din egen helse. Hvis du er usikker på hva du skal svare, vennligst svar så godt du kan.

Er din helse slik at den begrenser deg i utførelsen av disse aktivitetene NÅ?

Moderate aktiviteter som å flytte bord, støvsuge, gå en tur eller drive med hagearbeid:

Ja, begrenser meg mye	Ja, begrenser meg litt	Nei, begrenser meg ikke i det hele tatt
☐	☐	☐

Gå opp trappen flere etasjer:

Ja, begrenser meg mye	Ja, begrenser meg litt	Nei, begrenser meg ikke i det hele tatt
☐	☐	☐

I løpet av de siste 4 ukene, har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av din fysiske helse?	JA	NEI
Du har utrettet mindre enn du hadde ønsket	☐	☐
Du har vært hindret i å utføre visse typer arbeid eller gjøremål	☐	☐

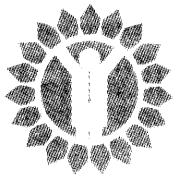
I løpet av de siste 4 ukene, har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål p.g.a. følelsesmessige problemer? *(Som f.eks. å være deprimert eller engstelig)*	JA	NEI
Du har utrettet mindre enn du hadde ønsket	☐	☐
Du har utført arbeidet eller andre gjøremål mindre grundig enn vanlig	☐	☐

I løpet av de siste 4 ukene, hvor mye har smerter påvirket ditt vanlige arbeid? *(Gjelder både i og utenfor hjemmet)* Sett bare ett kryss.	JA
Ikke i det hele tatt	☐ 1
Litt	☐ 2
En del	☐ 3
Mye	☐ 4
Svært mye	☐ 5

Hvor ofte i løpet av de siste 4 ukene har du følt deg rolig og harmonisk? Sett bare ett kryss.	JA
Hele tiden	☐ 1
Nesten hele tiden	☐ 2
Mye av tiden	☐ 3
En del av tiden	☐ 4
Litt av tiden	☐ 5
Ikke i det hele tatt	☐ 6

HELSEUNDERSØKELSEN I HORDALAND 1997-99

☐ Adresse endring



Ola Nordmann
SHUSvn. 1
5000 BERGEN

BERGEN 01 1 010150 44241

Personlig innbydelse

Kjære Ola Nordmann!

Hjertet ditt er viktig! Derfor inviterer vi deg til Helseundersøkelsen i Hordaland, HUSK. Dette er en undersøkelse som vil belyse ulike sider av helse og sykdom, med hovedvekt på forebyggelse av hjerte- og karsykdom. I brosjyren kan du lese mer om undersøkelsen. Alle som er født i 1953 - 57 og et utvalg født 1950 - 51 og 1925 - 27 blir invitert.

Vi har tildelt deg denne fremmøtetiden.

Tid: **torsdag 4. februar kl. 12.30 - 13.00**

Sted: Daniel Hansens gt. 9, 5. etasje (heis) - se vedlagt kart

Kan du ikke komme på dette tidspunktet, er du velkommen til en annen tid som passer deg. I så fall behøver du ikke gi oss beskjed; det er bare å møte når vi holder åpent.

Åpningstidene t.o.m. 26. mars 1999 er:

mandag og torsdag	kl 1130-1430 og 1530-1830
tirsdag og onsdag	kl 0800-1100 og 1200-1500
fredag	kl 0800-1300

Ved å ringe telefon 55 56 04 30, vil du kunne få nærmere orientering om undersøkelsen.

For de yngste deltakerne (årskullene 53 - 57, 50 - 51) tar undersøkelsen 10 - 15 minutter, men ventetiden kan variere noe. Et utvalg født i 50 - 51 blir i tillegg forespurt om deltakelse i en lungekapasitetsprøve, som tar ca. 20 minutter. Dette tilbudet blir også gitt til noen av de eldste deltakerne (født 25 - 27). De blir dessuten invitert til å delta i et intervju om hukommelse og minne, som tar ca. 30 minutter.

Møt til Helseundersøkelsen selv om du kjenner deg frisk, om du er under legebehandling, eller om du har målt kolesterol og blodtrykk nylig. På side 3 i brosjyren står det hva blodprøven omfatter. I tillegg blir alle prøvene analysert for kreatinin, som er et mål på nyrefunksjon. For deltakere født i 1925 - 27 og 1950 - 51 blir homocysteinnivået i blodet målt. I tillegg får de tilbud om å komme til Haukeland sykehus for å få målt bentetthet, som er et mål på benskjørhet (osteoporose).

4 - 6 uker etter undersøkelsen får du et brev med dine resultater, og eventuell melding dersom videre undersøkelse anbefales.

Egenandelen er kr 40,- (for dem som er 70 år eller eldre: kr 20,-). Vi kan dessverre ikke betale reisen eller utgifter til parkering.

Vi ber deg om å fylle ut spørreskjemaet på de neste sidene. Ta det med når du kommer til undersøkelsen.

HVA SPISER DU?

I dette skjemaet spør vi om dine spisevaner slik de **vanligvis** er. Vi er klar over at kostholdet varierer fra dag til dag. Prøv derfor så godt du kan å gi et **"gjennomsnitt"** av dine spisevaner. Ha det siste året i tankene når du fyller ut skjemaet. Der du er usikker, anslå svaret.

Skjemaet skal leses av en maskin, og derfor er det viktig at du setter et tydelig kryss i avmerket rute.

Riktig markering er slik: ☒

Bruk helst bløt blyant. Feil kan da rettes med viskelær.
Kulepenn og svart tusjpenn kan også brukes.

Av hensyn til den maskinelle lesingen pass på at arkene ikke blir brettet.

Alle svar vil bli behandlet strengt fortrolig.

EKSEMPEL PÅ UTFYLLING AV SPØRSMÅL 1.

Kari Nordmann spiser daglig 5 skiver brød og ett knekkebrød. Hun spiser vanligvis kneippbrød, men i helgene blir det en del loff. I tillegg spiser hun ett knekkebrød hver dag. Hun fyller ut første spørsmål slik:

1. HVOR MYE BRØD PLEIER DU Å SPISE?

Legg sammen det du bruker til alle måltider i løpet av en dag.

(1/2 rundstykke = 1 skive, 1 baguett = 5 skiver, 1 ciabatta = 4 skiver)

	Antall skiver pr. dag												
	0	1/2	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød (loff, baguetter, fine rundstykker o.l.)	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mellomgrovt brød (lys helkorn, lys kneipp, lyst hj.bakt o.l.)	☐	☐	☐	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød (fiberkneipp, mørk kneipp, mørkt hj.bakt o.l.)	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Knekkebrød (kavring, grov skonrok o.l.)	☐	☐	☒	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr. dag = 6

Antall skiver pr. uke: 6 x 7 = 42 Tallet brukes i spørsmål 5.

1. HVOR MYE BRØD PLEIER DU Å SPISE?

Legg sammen det du bruker til alle måltider i løpet av en dag.

(1/2 rundstykke = 1 skive, 1 baguett = 5 skiver, 1 ciabatta = 4 skiver)

	Antall skiver pr. dag												
	0	1/2	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød (loff, baguetter, fine rundstykker o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mellomgrovt brød (lys helkorn, lys kneipp, lyst hj.bakt o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød (fiberkneipp, mørk kneipp, mørkt hj.bakt o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Knekkebrød (kavring, grov skonrok o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr. dag = _____

Antall skiver pr. uke: _____ x 7 = _____. Tallet brukes i spørsmål 5.

2. HVA PLEIER DU Å SMØRE PÅ BRØDET?

Merk av både for hverdag og helg, selv om du bruker det samme.

Hverdager		Lørdager, søndager
☐	Bruker ikke	☐
☐	Smør (meierismør)	☐
☐	Bremykt, Smøregod	☐
☐	Brelett	☐
☐	Soft, soyamargarin (pakke, beger)	☐
☐	Solsikke	☐
☐	Oliven	☐
☐	Vita	☐
☐	Olivero	☐
☐	Omega	☐
☐	Soft light	☐
☐	Vita lett	☐
☐	Annen margarin	☐

3. OM DU BRUKER FETT PÅ BRØD, HVOR MYE BRUKER DU?

En porsjonspakning på 12 g rekker til antall skiver

1 ☐

2 ☐

3 ☐

4 ☐

5 ☐

4. MELK SOM DRIKK

(1 glass = 1,5 dl)

	Drikker sjelden/ ikke	Antall glass pr. dag							
		1/2	1	2	3	4	5	6	7	8+
Helmelk, søt, sur	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettmelk, søt, sur	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettmelk, ekstra lett	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Skummet melk, søt, sur	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

5. PÅLEGGSSORTER

Bruk sum skiver pr. uke fra spørsmål 1.

Til antall skiver pr. uke

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29-35	36+
Brun ost, prim	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hvit ost, helfet, 27% fett (Jarlsberg, Norvegia o.l., smøreost; eske, tube)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hvit ost, halvfet, 16% fett (Jarlsberg, Norvegia o.l., smøreost; eske, tube)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ost med mer enn 27% fett (kremoster, Normanna, Ridderost)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29-35	36+
Leverpostei, vanlig	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Leverpostei, mager	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Servelat, vanlig	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett servelat, kalverull, kokt skinke, okserull o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Salt pølse, spekepølse (fårepølse, salami o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29-35	36+
Kaviar	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Makrell i tomat, røkt makrell	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sardiner, sursild, ansjos o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29-35	36+
Syltetøy, marmelade, frysetøy	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Honning, sirup, sjokolade-, nøttepålegg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29-35	36+
Grønnsaker som pålegg (agurk, tomat o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Frukt som pålegg (banan, eple o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Salater med majones	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Majones på smørbrød	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

6. EGG

Antall pr. uke

	0	Mindre enn 1	1	2	3-4	5-6	7	8+
(kokt, stekt, eggerøre, omelett)	☐	☐	☐	☐	☐	☐	☐	☐

7. FROKOSTGRYN, GRØT OG YOGHURT

Svar enten pr. måned **eller** pr. uke. <1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang				
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1	1 1/2	2	3+
Havregryn, kornblandinger (4-korn, usøtet müsli o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Cornflakes, puffet ris, havrenøtter o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
												1-2	3-4	5-6	7+
Havregrøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
												1	2	3-4	5+
Sukker til frokostgryn, grøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ts)	☐	☐	☐	☐
												1/2	1	1 1/2	2+
Yoghurt, naturell, frukt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐
												1/2	1	1 1/2	2+
Lettyoghurt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐
Go´morgen yoghurt inkl. müsli	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	1/2 ☐	1 ☐	1 1/2 ☐	2+ ☐
												3/4	1	2	3+
Melk søt, sur på gryn, grøt og dessert	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐

8. KAFFE OG TE

(1 kopp kaffe = 1,2 dl 1 kopp te = 2 dl)

	Drikker ikke/ikke daglig	Antall kopper pr. dag: 1/2	1	2	3-4	5-6	7-8	9-10	11+
Kaffe, kokt	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe, traktet, filter	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe, pulver (instant)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe, koffeinfri	☐	☐	☐	☐	☐	☐	☐	☐	☐
Te	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nypete, urtete	☐	☐	☐	☐	☐	☐	☐	☐	☐

	Antall teskjeer eller biter pr. kopp: 0	1/2	1	2	3	4+
Sukker til kaffe	☐	☐	☐	☐	☐	☐
Sukker til te	☐	☐	☐	☐	☐	☐
Kunstig søtstoff til kaffe eller te	☐	☐	☐	☐	☐	☐
Fløte til kaffe	☐	☐	☐	☐	☐	☐

9. ANDRE DRIKKER?

Svar enten pr. måned **eller** pr. uke. < 1 betyr sjeldnere enn 1 gang.
Merk at porsjonsenhetene er forskjellige. 1/3 liter tilsvarer en halvflaske øl og 2/3 liter tilsvarer en helflaske.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang					
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3	4	5+
Vann	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Appelsinjuice	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Annen juice, most, nektar	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Saft, solbærsirup m. sukker	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Saft, kunstig søtet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., med sukker	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., kunstig søtet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	☐	☐	☐	☐	☐	☐
Farris, Selters, Soda o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	☐	☐	☐	☐	☐	☐
Alkoholfritt øl, vørterøl, lettøl	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	☐	☐	☐	☐	☐	☐
Pilsnerøl	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	☐	☐	☐	☐	☐	☐
Vin	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Brennevin, likør	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(1 dram = 4 cl)	☐	☐	☐	☐	☐	☐

	1/2	1	2	3	4	5+
Vann	☐	☐	☐	☐	☐	☐
Appelsinjuice	☐	☐	☐	☐	☐	☐
Annen juice, most, nektar	☐	☐	☐	☐	☐	☐
Saft, solbærsirup m. sukker	☐	☐	☐	☐	☐	☐
Saft, kunstig søtet	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., med sukker	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., kunstig søtet	☐	☐	☐	☐	☐	☐
Farris, Selters, Soda o.l.	☐	☐	☐	☐	☐	☐
Alkoholfritt øl, vørterøl, lettøl	☐	☐	☐	☐	☐	☐
Pilsnerøl	☐	☐	☐	☐	☐	☐
Vin	☐	☐	☐	☐	☐	☐
Brennevin, likør	☐	☐	☐	☐	☐	☐

	1/4	1/3	1/2	2/3	1	11/2+
Vann	☐	☐	☐	☐	☐	☐
Appelsinjuice	☐	☐	☐	☐	☐	☐
Annen juice, most, nektar	☐	☐	☐	☐	☐	☐
Saft, solbærsirup m. sukker	☐	☐	☐	☐	☐	☐
Saft, kunstig søtet	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., med sukker	☐	☐	☐	☐	☐	☐
Brus, Cola, Solo o.l., kunstig søtet	☐	☐	☐	☐	☐	☐
Farris, Selters, Soda o.l.	☐	☐	☐	☐	☐	☐
Alkoholfritt øl, vørterøl, lettøl	☐	☐	☐	☐	☐	☐
Pilsnerøl	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	6+
Vin	☐	☐	☐	☐	☐	☐
Brennevin, likør	☐	☐	☐	☐	☐	☐

10. MIDDAGSRETTER

Vi spør både om middagsmåltidene og det du spiser til andre måltider. Tell til slutt sammen antall retter du har merket for og se om summen virker sannsynlig.
En "dl" tilsvarer omtrent mengden i en suppeøse. Med "ss" menes en spiseskje.

	Gang pr. måned										Mengde pr. gang					
	0	<1	1	2	3	4	5-6	7-8	9+		1/2	2/3	1	11/2	2+	
Kjøttpølse, medisterpølse	☐	☐	☐	☐	☐	☐	☐	☐	☐	(kjøttpølse)	☐	☐	☐	☐	☐	
Hamburger, karbonader o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Grill- og wienerpølse	☐	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Hamburger-, pølsebrød, lomper	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Kjøttkaker, medisterkaker, kjøttpudding	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Kjøttdeigretter (saus eller gryte med kjøttdeig, lasagne o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Taco (med kjøtt og salat)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Pastaretter	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	

	Gang pr. måned										Mengde pr. gang				
	0	<1	1	2	3	4	5-6	7-8	9+		1/8	1/4	1/2	3/4	1+
Pizza (500-600 g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(pizza)	☐	☐	☐	☐	☐
											1/2	1	1 1/2	2	2 1/2+
Biff (alle typer kjøtt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1/2	1	1 1/2	2	2 1/2+
Koteletter (lam, okse, svin)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1-2	3-4	5-6	7-8	9+
Stek (lam, okse, svin)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
											1-2	3-4	5-6	7-8	9+
Stek (elg, hjort, reinsdyr o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
Gryterett med helt kjøtt, frikassé, fårikål o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Lapskaus, suppelapskaus, betasuppe	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
											1-2	3-4	5-6	7-8	9+
Bacon, stekt flesk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
											1/4	1/3	1/2	3/4	1+
Kylling, høne	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1-2	3-4	5-6	7-8	9+
Leverretter	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
	0	<1	1	2	3	4	5-6	7-8	9+		1	2	3	4	5+
Fiskekaker, fiskepudding, fiskeboller	☐	☐	☐	☐	☐	☐	☐	☐	☐	(kake)	☐	☐	☐	☐	☐
											1-2	3-4	5-6	7-9	10+
Fiskepinner	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Torsk, sei, hyse (kokt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Torsk, sei, hyse (stekt, panert)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Sild (fersk, speket, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	☐	☐	☐	☐	☐
											1/2	1	1 1/2	2	3+
Makrell (fersk, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Laks, ørret (sjø, oppdrett)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	☐	☐	☐	☐	☐
Fiskegryte, -grateng, suppe med fisk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
											1	2	3	4	5+
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl, renset)	☐	☐	☐	☐	☐
	0	<1	1	2	3	4	5-6	7-8	9+		1-2	3-4	5-6	7-8	9+
Risgrøt, annen melkegrøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
											1-2	3-4	5-6	7-8	9+
Pannekaker	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
Suppe (tomat, blomkål, ertesuppe o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Vegetarrett, vegetarpizza grønnsakgrateng, -pai	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bit/dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
	0	<1	1	2	3	4	5-6	7-8	9+		1/2	1	1 1/2	2	2 1/2+
Brun/hvit saus	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Smeltet margarin, smør til fisk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
											1	2	3	4	5+
Bearnaisesaus o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Majones, remulade	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	☐	☐	☐	☐	☐
											1	2	3	4	5+
Ketchup	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	☐	☐	☐	☐	☐

11. POTETER, RIS, SPAGHETTI, GRØNNSAKER

Svar enten pr. måned **eller** pr. uke. <1 betyr sjeldnere enn 1 gang.
Disse spørsmålene dreier seg først og fremst om tilbehør til middagsretter, men spiser du for eksempel en rå gulrot eller salat til lunsj, skal det tas med her.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang				
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1	2	3	4	5+
Poteter, kokte	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
Pommes frites, stekte poteter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Potetmos, -stuing, gratinerte poteter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Ris	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Spaghetti, makaroni, pasta	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Gulrot	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	1 1/2 ☐	2 ☐	3+ ☐
Hodekål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skalk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kålrot	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Blomkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bukett)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Brokkoli	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bukett)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Rosenkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Grønnkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Løk	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Spinat, andre bladgrønns.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Sopp	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Avocado	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/4 ☐	1/2 ☐	3/4 ☐	1 ☐	1 1/4 + ☐
Paprika	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(strimmel)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Tomat	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	1 1/2 ☐	2 ☐	3+ ☐
Tomatbønner, bønner/linser	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Mais	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Erter, frosne grønnsak-blandinger	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Salatblandinger	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Dressing	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Rømme	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐

Hvor mange ganger om dagen spiser du vanligvis grønnsaker utenom grønnsakene du spiser til middag?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+ ☐

12. TYPE FETT TIL MATLAGING

Smør/margarin	Oljer
☐ Smør (meierismør)	☐ Olivenolje
☐ Bremykt	☐ Soyaolje
☐ Melange, Per	☐ Maisolje
☐ Soft-, soyamargarin (pakke, beger)	☐ Solsikkeolje
☐ Solsikke	☐ Valnøttolje
☐ Oliven	☐ Andre oljer
☐ Annen margarin	

13. FRUKT

Svar enten pr. måned **eller** pr. uke. < 1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang			
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3+
Eple	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Appelsin, mandarin, grapefrukt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Banan	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Druer	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(klase)	☐	☐	☐	☐
Eksotisk frukt (kiwi, mango)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Annen frukt (fersken, pære m.v.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Jordbær, bringebær (friske, frosne)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Blåbær	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Multer	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐

Hvor mange frukter spiser du vanligvis pr. dag?

0	1	2	3	4	5	6	7	8	9+
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

14. DESSERT, KAKER, GODTERI

Svar enten pr. måned **eller** pr. uke. < 1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang			
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3+
Hermetisk frukt, fruktgrøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Puddinger (sjokolade, karamell o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Is (1 dl = 1 pinne = 1 kremmerhus)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Boller, julekake, kringle	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Skolebrød, skillingsbolle	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Wienerbrød, -kringle o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Smultring, formkake	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Vafler	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(plate)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Sjokoladekake, bløtkake, annen fylt kake	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Søt kjeks, kakekjeks (Cookies, Bixit, Hob Nobs)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Sjokolade (60 g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(plate)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Drops, lakris, seigmenn o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Smågodt (1 hg = 100g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(hg)	1/2 ☐	3/4 ☐	1 ☐	1 1/2+ ☐
Potetgull (1 pose 100g = 7 dl)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Annen snacks (skruer, crisp, saltstenger, lettsnacks o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Peanøtter, andre nøtter (1 pose 100g = 4 never)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(neve)	1 ☐	2 ☐	3 ☐	4+ ☐

15. KOSTTILSKUDD (bs = barneskje, ts = teskje)

	Hele året	Bare vinter-halvåret	Gang pr. uke: 0	<1	1	2-3	4-5	6-7		Mengde pr. gang			
										1 ts	1 bs	1 ss	
Tran	☐	☐	☐	☐	☐	☐	☐	☐		☐	☐	☐	
										1	2+		
Trankapsler	☐	☐	☐	☐	☐	☐	☐	☐	kapsler	☐	☐		
										1-2	3-4	5-6	7+
Fiskeoljekapsler	☐	☐	☐	☐	☐	☐	☐	☐	kapsler	☐	☐	☐	☐
Multipreparater													
			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Sanasol	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Biovit	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Vitaplex	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Kostpluss	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Vitamineral	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Hvis annet, hvilket? .....

Jernpreparater													
			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Ferro C	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Hemofer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Duroferon Duretter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Hvis annet, hvilket? .....

			0	<1	1	2-3	4-5	6-7		1	2	3	4+
B-vitaminer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
C-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
D-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
E-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Folat (folsyre)	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Kalktabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Fluortabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Hvis annet, hvilket? .....

16. NÅR SPISER DU PÅ HVERDAGER?

HOVEDMÅLTIDER som frokost, formiddagsmat, middag, kvelds.

Omtrent klokken

6		8		10		12		14		16		18		20		22		24		2		4
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

MELLOMMÅLTIDER som kaffe, frukt, godteri, snacks m.v.

Omtrent klokken

6		8		10		12		14		16		18		20		22		24		2		4
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

17. MENER DU SVARENE I SPØRRESKJEMAET GIR ET BRUKBART BILDE AV KOSTHOLDET DITT?

Ja ☐ Nei ☐

Er det matvarer/produkter du regelmessig bruker, og som ikke er nevnt i skjemaet?

.....

.....

18. ER DU FORNØYD MED KROPPSVEKTEN DIN SLIK DEN ER NÅ?

- ☐ Ja
- ☐ Nei, jeg ønsker å slanke meg
- ☐ Nei, jeg ønsker å legge på meg

19. KJØNN

Mann ☐ Kvinne ☐

Vennligst se etter at du har svart på alle spørsmål.

Takk for innsatsen!

HUSK DELPROSJEKT: HUKOMMELSE OG MINNE

	Maksimal skår	Skår
1. Hvilket år er det?	1	
2. Hvilken måned er det?	1	
3. Hvilken dato er det i dag?	1	
4. Hvilken dag er det i dag?	1	
5. I hvilken landsdel er vi nå?	1	
6. Hva er postnummeret ditt?	1	

Si 3 ord, OST - SYKKEL - BOK, langsomt,
1 sekund mellom hver. Be pasienten gjenta dem
etter deg til han/hun har lært dem. Ikke gi poeng her.

	Maksimal skår	Skår
7. Be pasienten stave ordet SVERD baklengs. Gi ett poeng hvis det er tre eller flere riktige bokstaver sagt i rett rekkefølge.	1	
8. Kan du si meg de ordene du skulle huske for litt siden? (OST - SYKKEL - BOK). Gi ett poeng hvis pasienten klarer minst ett ord.	1	
9. Gjenta følgende setning: «Aldri annet enn om og men».	1	
10. Utfør følgende: Ta et stykke papir med din høyre hånd, brett det over på midten, og legg det på gulvet. Gi ett poeng hvis alt er gjort riktig.	1	
11. Skriv en setning. (skal inneholde subjekt og predikat).	1	
12. Kopier denne tegningen.	1	
	Total skår	12

Intervjuer:

Symbol Digit Modalities Test

Kendrick

Generating first names

Block design

Trail making

HAD

Rettledning

Her kommer noen spørsmål om hvorledes du føler seg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser **den siste uken**.
Ikke tenk for lenge på svaret – de spontane svarene er best.

1. Jeg føler meg nervøs og urolig

- 3 –Mesteparten av tiden
- 2 –Mye av tiden
- 1 –Fra tid til annen
- 0 –Ikke i det hele tatt

2. Jeg gleder meg fortsatt over tingene slik jeg pleide før

- 0 –Avgjort like mye
- 1 –Ikke fullt så mye
- 2 –Bare lite grann
- 3 –Ikke i det hele tatt

3. Jeg har en urofølelse som om noe forferdelig vil skje

- 3 –Ja, og noe svært ille
- 2 –Ja, ikke så veldig ille
- 1 –Litt, bekymrer meg lite
- 0 –Ikke i det hele tatt

4. Jeg kan le og se det morsomme i situasjoner

- 0 –Like mye nå som før
- 1 –Ikke like mye nå som før
- 2 –Avgjort ikke som før
- 3 –Ikke i det hele tatt

5. Jeg har hodet fullt av bekymringer

- 3 –Veldig ofte
- 2 –Ganske ofte
- 1 –Av og til
- 0 –En gang i blant

6. Jeg er i godt humør

- 3 –Aldri
- 2 –Noen ganger
- 1 –Ganske ofte
- 0 –For det meste

7. Jeg kan sitte i fred og ro og kjenne meg avslappet

- 0 –Ja, helt klart
- 1 –Vanligvis
- 2 –Ikke så ofte
- 3 –Ikke i det hele tatt

8. Jeg føler meg som om alt går langsommere

- 3 –Nesten hele tiden
- 2 –Svært ofte
- 1 –Fra tid til annen
- 0 –Ikke i det hele tatt

9. Jeg føler meg urolig som om jeg har sommerfugler i magen

- ☐ 0 –Ikke i det hele tatt
- ☐ 1 –Fra tid til annen
- ☐ 2 –Ganske ofte
- ☐ 3 –Svært ofte

10. Jeg bryr meg ikke lenger om hvordan jeg ser ut

- ☐ 3 –Ja, jeg har sluttet å bry meg
- ☐ 2 –Ikke som jeg burde
- ☐ 1 –Kan hende ikke nok
- ☐ 0 –Bryr meg som før

11. Jeg er rastløs som om jeg stadig må være aktiv

- ☐ 3 –Uten tvil svært mye
- ☐ 2 –Ganske mye
- ☐ 1 –Ikke så veldig mye
- ☐ 0 –Ikke i det hele tatt

12. Jeg ser med glede frem til hendelser og ting

- ☐ 0 –Like mye som før
- ☐ 1 –Heller mindre enn før
- ☐ 2 –Avgjort mindre enn før
- ☐ 3 –Nesten ikke i det hele tatt

13. Jeg kan plutselig få en følelse av panikk

- ☐ 3 –Uten tvil svært ofte
- ☐ 2 –Ganske ofte
- ☐ 1 –Ikke så veldig ofte
- ☐ 0 –Ikke i det hele tatt

14. Jeg kan glede meg over gode bøker, radio og TV

- ☐ 0 –Ofte
- ☐ 1 –Fra tid til annen
- ☐ 2 –Ikke så ofte
- ☐ 3 –Svært sjelden